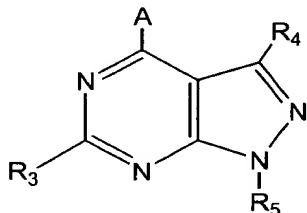


CLAIMS

The invention that is claimed is:

5 1. A pharmaceutical composition comprising a corticotropin releasing factor antagonist and a growth hormone secretagogue or growth hormone.

2. A pharmaceutical composition according to claim 1 wherein said corticotropin releasing factor antagonist is a compound of formula



10 or a pharmaceutically acceptable acid addition salt thereof, wherein A is NR<sub>1</sub>R<sub>2</sub>, CR<sub>1</sub>R<sub>2</sub>R<sub>11</sub>, or C(=CR<sub>1</sub>R<sub>12</sub>)R<sub>2</sub>, NHCR<sub>1</sub>R<sub>2</sub>R<sub>11</sub>, OCR<sub>1</sub>R<sub>2</sub>R<sub>11</sub>, SCR<sub>1</sub>R<sub>2</sub>R<sub>11</sub>, NHNR<sub>1</sub>R<sub>2</sub>, CR<sub>2</sub>R<sub>11</sub>NHR<sub>1</sub>, CR<sub>2</sub>R<sub>11</sub>OR<sub>1</sub>, CR<sub>2</sub>R<sub>11</sub>SR<sub>1</sub> or C(O)R<sub>2</sub>;  
R<sub>1</sub> is hydrogen, or C<sub>1</sub>-C<sub>6</sub> alkyl which may be substituted by one or two  
15 substituents R<sub>6</sub> independently selected from the group consisting of hydroxy, fluoro, chloro, bromo, iodo, C<sub>1</sub>-C<sub>6</sub> alkoxy, O-C(O)-(C<sub>1</sub>-C<sub>6</sub> alkyl), O-C(O)-N(C<sub>1</sub>-C<sub>4</sub> alkyl)(C<sub>1</sub>-C<sub>2</sub> alkyl); amino, NH(C<sub>1</sub>-C<sub>4</sub> alkyl), S(C<sub>1</sub>-C<sub>6</sub> alkyl), OC(O)NH(C<sub>1</sub>-C<sub>4</sub> alkyl), N(C<sub>1</sub>-C<sub>2</sub> alkyl)C(O)(C<sub>1</sub>-C<sub>4</sub> alkyl), NHC(O)(C<sub>1</sub>-C<sub>4</sub> alkyl), COOH, CO(C<sub>1</sub>-C<sub>4</sub> alkyl), C(O)NH(C<sub>1</sub>-C<sub>4</sub> alkyl), C(O)N(C<sub>1</sub>-C<sub>4</sub> alkyl)(C<sub>1</sub>-C<sub>2</sub> alkyl), SH, CN, NO<sub>2</sub>, SO(C<sub>1</sub>-C<sub>4</sub> alkyl); SO<sub>2</sub>(C<sub>1</sub>-C<sub>4</sub> alkyl), SO<sub>2</sub>NH(C<sub>1</sub>-C<sub>4</sub> alkyl), SO<sub>2</sub>N(C<sub>1</sub>-C<sub>4</sub> alkyl)(C<sub>1</sub>-C<sub>2</sub> alkyl), and said C<sub>1</sub>-C<sub>6</sub> alkyl may  
20 have one or two double or triple bonds;  
R<sub>2</sub> is C<sub>1</sub>-C<sub>12</sub> alkyl, aryl or (C<sub>1</sub>-C<sub>10</sub> alkylene)aryl wherein said aryl is phenyl, naphthyl, thienyl, benzothienyl, pyridyl, quinolyl, pyrazinolyl, pyrimidyl, imidazolyl, furanyl, benzofuranyl, benzothiazolyl, isothiazolyl, benzisothiazolyl, thiazolyl,  
25 isoxazolyl, benzisoxazolyl, benzimidazolyl, triazolyl, pyrazolyl, pyrrolyl, indolyl, azaindolyl, oxazolyl, or benzoxazolyl; 3- to 8-membered cycloalkyl or (C<sub>1</sub>-C<sub>6</sub> alkylene) cycloalkyl, wherein said cycloalkyl may have one or two of O, S or N-Z, wherein Z is hydrogen, substituted, independently, for one or two carbons of said cycloalkyl, C<sub>1</sub>-C<sub>4</sub> alkyl, benzyl or C<sub>1</sub>-C<sub>4</sub> alkanoyl, wherein R<sup>2</sup> may be substituted independently by  
30 from one to three of chloro, fluoro, or C<sub>1</sub>-C<sub>4</sub> alkyl, or one of hydroxy, bromo, iodo, C<sub>1</sub>-

C<sub>6</sub> alkoxy, OC(O)(C<sub>1</sub>-C<sub>6</sub> alkyl), O-C-N(C<sub>1</sub>-C<sub>4</sub> alkyl)(C<sub>1</sub>-C<sub>2</sub> alkyl), S(C<sub>1</sub>-C<sub>6</sub> alkyl), NH<sub>2</sub>, NH(C<sub>1</sub>-C<sub>2</sub> alkyl), N(C<sub>1</sub>-C<sub>4</sub> alkyl) C(O)(C<sub>1</sub>-C<sub>4</sub> alkyl), NHC(O)(C<sub>1</sub>-C<sub>4</sub> alkyl), COOH, C(O)O(C<sub>1</sub>-C<sub>4</sub> alkyl), C(O)NH(C<sub>1</sub>-C<sub>4</sub> alkyl), C(O)N(C<sub>1</sub>-C<sub>4</sub> alkyl)(C<sub>1</sub>-C<sub>2</sub> alkyl), SH, CN, NO<sub>2</sub>, SO(C<sub>1</sub>-C<sub>4</sub> alkyl), SO<sub>2</sub>(C<sub>1</sub>-C<sub>4</sub> alkyl), SO<sub>2</sub>NH(C<sub>1</sub>-C<sub>4</sub> alkyl), SO<sub>2</sub>N(C<sub>1</sub>-C<sub>4</sub> alkyl)(C<sub>1</sub>-C<sub>2</sub>

5 alkyl), and wherein said C<sub>1</sub>-C<sub>12</sub> alkyl or C<sub>1</sub>-C<sub>10</sub> alkylene may have one to three double or triple bonds; or

NR<sub>1</sub>R<sub>2</sub> or CR<sub>1</sub>R<sub>2</sub>R<sub>11</sub> may form a 4- to 8-membered ring optionally having one or two double bonds or one or two of O, S or N-Z wherein Z is hydrogen, C<sub>1</sub>-C<sub>4</sub> alkyl, benzyl, or C<sub>1</sub>-C<sub>4</sub> alkanoyl;

10 R<sub>3</sub> is hydrogen, C<sub>1</sub>-C<sub>6</sub> alkyl, fluoro, chloro, bromo, iodo, hydroxy, amino, O(C<sub>1</sub>-C<sub>6</sub> alkyl), NH(C<sub>1</sub>-C<sub>6</sub> alkyl), N(C<sub>1</sub>-C<sub>4</sub> alkyl)(C<sub>1</sub>-C<sub>2</sub> alkyl), SH, S(C<sub>1</sub>-C<sub>4</sub> alkyl), SO(C<sub>1</sub>-C<sub>4</sub> alkyl), or SO<sub>2</sub>(C<sub>1</sub>-C<sub>4</sub> alkyl), wherein said C<sub>1</sub>-C<sub>4</sub> alkyl and C<sub>1</sub>-C<sub>6</sub> alkyl may have one or two double or triple bonds and may be substituted by from 1 to 3 R<sub>7</sub> substituents independently selected from the group consisting of hydroxy, amino, C<sub>1</sub>-C<sub>3</sub> alkoxy, 15 dimethylamino, diethylamino, methylamino, ethylamino, NHC(O)CH<sub>3</sub>, fluoro, chloro or C<sub>1</sub>-C<sub>3</sub> thioalkyl;

20 R<sub>4</sub> is hydrogen, C<sub>1</sub>-C<sub>6</sub> alkyl, fluoro, chloro, bromo, iodo, C<sub>1</sub>-C<sub>6</sub> alkoxy, amino, NH(C<sub>1</sub>-C<sub>6</sub> alkyl), N(C<sub>1</sub>-C<sub>6</sub> alkyl) (C<sub>1</sub>-C<sub>2</sub> alkyl), SO<sub>n</sub>(C<sub>1</sub>-C<sub>6</sub> alkyl), wherein n is 0, 1 or 2, cyano, hydroxy, carboxy, or amido, wherein said C<sub>1</sub>-C<sub>6</sub> alkyls may be substituted by one to three of hydroxy, amino, carboxy, amido, NHC(O)(C<sub>1</sub>-C<sub>4</sub> alkyl), NH(C<sub>1</sub>-C<sub>4</sub> alkyl), N(C<sub>1</sub>-C<sub>4</sub> alkyl)(C<sub>1</sub>-C<sub>2</sub> alkyl), C(O)O(C<sub>1</sub>-C<sub>4</sub> alkyl), C<sub>1</sub>-C<sub>3</sub> alkoxy, C<sub>1</sub>-C<sub>3</sub> thioalkyl, fluoro, bromo, chloro, iodo, cyano or nitro;

25 R<sub>5</sub> is phenyl, naphthyl, thienyl, benzothienyl, pyridyl, quinolyl, pyrazinolyl, pyrimidyl, imidazolyl, furanyl, benzofuranyl, benzothiazolyl, isothiazolyl, benzoisothiazolyl, thiazolyl, isoxazolyl, benzisoxazolyl, benzimidazolyl, triazolyl, pyrazolyl, pyrrolyl, indolyl, pyrrolopyridyl benzoxazolyl, oxazolyl, pyrrolidinyl, thiazolidinyl, piperazinyl, piperidinyl, or tetrazolyl, wherein each one of the above groups may be substituted independently by from one to three of fluoro, chloro, bromo, formyl, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkoxy or trifluoromethyl, or one of hydroxy, iodo, 30 cyano, nitro, amino, cyclopropyl, NH(C<sub>1</sub>-C<sub>4</sub> alkyl), N(C<sub>1</sub>-C<sub>4</sub> alkyl)(C<sub>1</sub>-C<sub>2</sub> alkyl), COO(C<sub>1</sub>-C<sub>4</sub> alkyl), CO(C<sub>1</sub>-C<sub>4</sub> alkyl), SO<sub>2</sub>NH(C<sub>1</sub>-C<sub>4</sub> alkyl), SO<sub>2</sub>N(C<sub>1</sub>-C<sub>4</sub> alkyl)(C<sub>1</sub>-C<sub>2</sub> alkyl), SO<sub>2</sub>NH<sub>2</sub>, NHSO<sub>2</sub>(C<sub>1</sub>-C<sub>4</sub> alkyl), S(C<sub>1</sub>-C<sub>6</sub> alkyl), SO<sub>2</sub>(C<sub>1</sub>-C<sub>6</sub> alkyl), wherein said C<sub>1</sub>-C<sub>4</sub> alkyl and C<sub>1</sub>-C<sub>6</sub> alkyl may have one double or triple bond and may be

substituted by one or two of fluoro, chloro, hydroxy, amino, methylamino, dimethylamino or acetyl; with the proviso that  $R_5$  is not unsubstituted phenyl;

$R_{11}$  is hydrogen, hydroxy, fluoro, chloro,  $\text{COO}(\text{C}_1\text{-C}_2\text{ alkyl})$ , cyano, or  $\text{CO}(\text{C}_1\text{-C}_2\text{ alkyl})$ ; and

5  $R_{12}$  is hydrogen or  $\text{C}_1\text{-C}_4$  alkyl;

with the provisos that:

(a) A is not straight chain  $\text{C}_1\text{-C}_{12}$  alkyl;

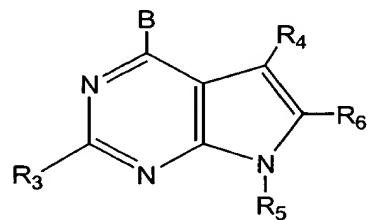
(b) when  $R_3$  is hydrogen, A is benzyl or phenethyl, and  $R_4$  is fluoro, chloro, bromo or iodo, then  $R_5$  is not 5'-deoxy-ribofuranosyl or 5'-amino-5'-deoxy-

10 ribofuranosyl; and

(c) when  $R^5$  is phenyl, said phenyl is substituted by two or three substituents.

3. A pharmaceutical composition according to claim 1 wherein said

15 corticotropin releasing factor antagonist is a compound of formula



and the pharmaceutically acceptable acid addition salts thereof, wherein

B is  $\text{NR}_1\text{R}_2$ ,  $\text{CR}_1\text{R}_2\text{R}_{11}$ ,  $\text{C}(\text{=CR}_2\text{R}_{12})\text{R}_1$ ,  $\text{NHR}_1\text{R}_2\text{R}_{11}$ ,  $\text{OCR}_1\text{R}_2\text{R}_{11}$ ,  $\text{SCR}_1\text{R}_2\text{R}_{11}$ ,  $\text{NHNR}_1\text{R}_2$ ,  $\text{CR}_2\text{R}_{11}\text{NHR}_1$ ,  $\text{CR}_2\text{R}_{11}\text{OR}_1$ ,  $\text{CR}_2\text{R}_{11}\text{SR}_1$ , or  $\text{C}(\text{O})\text{R}_2$ ;

20  $R_1$  is hydrogen, or  $\text{C}_1\text{-C}_6$  alkyl which may be substituted by one or two

substituents  $R_7$  independently selected from the group consisting of hydroxy, fluoro, chloro, bromo, iodo,  $\text{C}_1\text{-C}_8$  alkoxy,  $\text{O-C(=O)-(C}_1\text{-C}_6\text{ alkyl)}$ ,  $\text{O-C(=O)NH(C}_1\text{-C}_4\text{ alkyl)}$ ,  $\text{O-C(=O)-N(C}_1\text{-C}_4\text{ alkyl)(C}_1\text{-C}_2\text{ alkyl)}$ , amino,  $\text{NH(C}_1\text{-C}_4\text{ alkyl)}$ ,  $\text{N(C}_1\text{-C}_2\text{ alkyl)(C}_1\text{-C}_4\text{ alkyl)}$ ,  $\text{S(C}_1\text{-C}_6\text{ alkyl)}$ ,  $\text{N(C}_1\text{-C}_4\text{ alkyl)C(=O)(C}_1\text{-C}_4\text{ alkyl)}$ ,  $\text{NH(C}_1\text{-C}_4\text{ alkyl)}$ ,  $\text{COOH}$ ,  $\text{C(=O)O(C}_1\text{-C}_4\text{ alkyl)}$ ,  $\text{C(=O)NH(C}_1\text{-C}_4\text{ alkyl)}$ ,  $\text{C(=O)N(C}_1\text{-C}_4\text{ alkyl)(C}_1\text{-C}_2\text{ alkyl)}$ ,  $\text{SH}$ ,  $\text{CN}$ ,  $\text{NO}_2$ ,

25  $\text{SO(C}_1\text{-C}_4\text{ alkyl)}$ ,  $\text{SO}_2(\text{C}_1\text{-C}_4\text{ alkyl)}$ ,  $\text{SO}_2\text{NH(C}_1\text{-C}_4\text{ alkyl)}$ ,  $\text{SO}_2\text{N(C}_1\text{-C}_4\text{ alkyl)(C}_1\text{-C}_2\text{ alkyl)}$ , and said  $\text{C}_1\text{-C}_6$  alkyl may contain one or two double or triple bonds;

$R_2$  is  $\text{C}_1\text{-C}_{12}$  alkyl, aryl or  $(\text{C}_1\text{-C}_{10}$  alkylene)aryl wherein said aryl is phenyl, naphthyl, thienyl, benzothienyl, pyridyl, quinolyl, pyrazinyl, pyrimidyl, imidazolyl,

30 furanyl, benzofuranyl, benzothiazolyl, isothiazolyl, benzisothiazolyl, thiazolyl,

isoxazolyl, benzisoxazolyl, benzimidazolyl, triazolyl, pyrazolyl, pyrrolyl, indolyl, pyrrolopyridyl, oxazolyl, or benzoxazolyl; 3- to 8-membered cycloalkyl or (C<sub>1</sub>-C<sub>6</sub> alkylene) cycloalkyl, wherein said cycloalkyl may contain one or two of O, S or N-Z wherein Z is hydrogen, C<sub>1</sub>-C<sub>4</sub> alkyl, benzyl or C<sub>1</sub>-C<sub>4</sub> alkanoyl, wherein R<sub>2</sub> may be

5 substituted independently by from one to three of chloro, fluoro, or C<sub>1</sub>-C<sub>4</sub> alkyl, or one of hydroxy, bromo, iodo, C<sub>1</sub>-C<sub>6</sub> alkoxy, O-C(=O)-(C<sub>1</sub>-C<sub>6</sub> alkyl), O-C-N(C<sub>1</sub>-C<sub>4</sub> alkyl)(C<sub>1</sub>-C<sub>2</sub> alkyl), S(C<sub>1</sub>-C<sub>6</sub> alkyl), NH<sub>2</sub>, NH(C<sub>1</sub>-C<sub>2</sub> alkyl), N(C<sub>1</sub>-C<sub>2</sub> alkyl) (C<sub>1</sub>-C<sub>4</sub> alkyl), N(C<sub>1</sub>-C<sub>4</sub>)-C(=O)(C<sub>1</sub>-C<sub>4</sub> alkyl), NHC(=O)(C<sub>1</sub>-C<sub>4</sub>), COOH, C(=O)O(C<sub>1</sub>-C<sub>4</sub> alkyl), C(=O)NH(C<sub>1</sub>-C<sub>4</sub> alkyl), C(=O)N(C<sub>1</sub>-C<sub>4</sub> alkyl)(C<sub>1</sub>-C<sub>2</sub> alkyl), SH, CN, NO<sub>2</sub>, SO(C<sub>1</sub>-C<sub>4</sub> alkyl), SO<sub>2</sub>(C<sub>1</sub>-C<sub>4</sub> alkyl), SO<sub>2</sub>NH(C<sub>1</sub>-C<sub>4</sub> alkyl), SO<sub>2</sub>N(C<sub>1</sub>-C<sub>4</sub> alkyl)(C<sub>1</sub>-C<sub>2</sub> alkyl), and wherein said C<sub>1</sub>-C<sub>12</sub> alkyl or C<sub>1</sub>-C<sub>10</sub> alkylene may contain one to three double or triple bonds; or

10 NR<sub>1</sub>R<sub>2</sub> or CR<sub>1</sub>R<sub>2</sub>R<sub>11</sub> may form a saturated 3- to 8 membered carbocyclic ring of which the 5- to 8-membered ring contain one or two double bonds or one or two of O, S or N-Z wherein Z is hydrogen, C<sub>1</sub>-C<sub>4</sub> alkyl, benzyl or C<sub>1</sub>-C<sub>4</sub> alkanoyl;

15 R<sub>3</sub> is hydrogen, C<sub>1</sub>-C<sub>6</sub> alkyl, fluoro, chloro, bromo, iodo, hydroxy, amino, O(C<sub>1</sub>-C<sub>6</sub> alkyl), NH(C<sub>1</sub>-C<sub>6</sub> alkyl), N(C<sub>1</sub>-C<sub>4</sub> alkyl)(C<sub>1</sub>-C<sub>2</sub> alkyl), SH, S(C<sub>1</sub>-C<sub>4</sub> alkyl), SO(C<sub>1</sub>-C<sub>4</sub> alkyl), or SO<sub>2</sub>(C<sub>1</sub>-C<sub>4</sub> alkyl), wherein said C<sub>1</sub>-C<sub>4</sub> alkyl and C<sub>1</sub>-C<sub>6</sub> alkyl may contain from one or two double or triple bonds and may be substituted by from 1 to 3 substituents R<sub>8</sub> independently selected from the group consisting of hydroxy, amino, C<sub>1</sub>-C<sub>3</sub> alkoxy,

20 dimethylamino, diethylamino, methylamino, ethylamino, NHCH<sub>3</sub>, fluoro, chloro or C<sub>1</sub>-C<sub>3</sub> thioalkyl;

R<sub>4</sub> and R<sub>6</sub> are each independently hydrogen, C<sub>1</sub>-C<sub>6</sub> alkyl, fluoro, chloro, bromo, iodo, C<sub>1</sub>-C<sub>6</sub> alkoxy, amino, NH(C<sub>1</sub>-C<sub>6</sub> alkyl), N(C<sub>1</sub>-C<sub>6</sub> alkyl)(C<sub>1</sub>-C<sub>2</sub> alkyl), SO<sub>n</sub>(C<sub>1</sub>-C<sub>6</sub> alkyl), wherein n is 0, 1 or 2, cyano, hydroxy, carboxy, or amido, wherein

25 said C<sub>1</sub>-C<sub>6</sub> alkyls may be substituted by one to three of hydroxy, amino, carboxy, amido, NHC(=O)(C<sub>1</sub>-C<sub>4</sub> alkyl), NH(C<sub>1</sub>-C<sub>4</sub> alkyl), N(C<sub>1</sub>-C<sub>4</sub> alkyl)(C<sub>1</sub>-C<sub>2</sub> alkyl), C(=O)O(C<sub>1</sub>-C<sub>4</sub> alkyl), C<sub>1</sub>-C<sub>3</sub> alkoxy, C<sub>1</sub>-C<sub>3</sub> thioalkyl, fluoro, bromo, chloro, iodo, cyano or nitro;

R<sub>5</sub> is phenyl, naphthyl, thienyl, benzothienyl, pyridyl, quinolyl, pyrazinyl,

30 pyrimidyl, imidazolyl, furanyl, benzofuranyl, benzothiazolyl, isothiazolyl, benzisothiazolyl, thiazolyl, isoxazolyl, benzisoxazolyl, benzimidazolyl, triazolyl, pyrazolyl, pyrrolyl, indolyl, azaindolyl, benzoxazolyl, oxazolyl, pyrrolidinyl, thiazolidinyl, morpholinyl, piperidinyl, piperazinyl, tetrazolyl, or 3- to 8-membered cycloalkyl or 9- to 12-membered bicycloalkyl, optionally containing one to three of O, S or N-Z wherein

Z is hydrogen, C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> alkanoyl, phenyl or phenylmethyl, wherein each one of the above groups may be substituted independently by from one to four of fluoro, chloro, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkoxy or trifluoromethyl, or one of bromo, iodo, cyano, nitro, amino, NH(C<sub>1</sub>-C<sub>4</sub> alkyl), N(C<sub>1</sub>-C<sub>4</sub>)(C<sub>1</sub>-C<sub>2</sub> alkyl), COO(C<sub>1</sub>-C<sub>4</sub> alkyl), CO(C<sub>1</sub>-C<sub>4</sub>

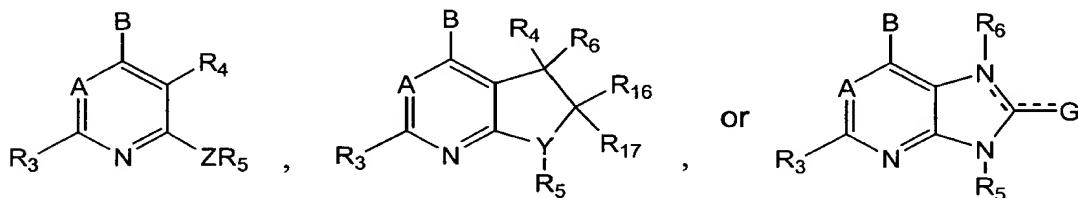
5 alkyl), SO<sub>2</sub>NH(C<sub>1</sub>-C<sub>4</sub> alkyl), SO<sub>2</sub>N(C<sub>1</sub>-C<sub>4</sub> alkyl)(C<sub>1</sub>-C<sub>2</sub> alkyl), SO<sub>2</sub>NH<sub>2</sub>, NSO<sub>2</sub>(C<sub>1</sub>-C<sub>4</sub> alkyl), S(C<sub>1</sub>-C<sub>6</sub> alkyl), SO<sub>2</sub>(C<sub>1</sub>-C<sub>6</sub> alkyl), wherein said C<sub>1</sub>-C<sub>4</sub> alkyl and C<sub>1</sub>-C<sub>6</sub> alkyl may be substituted by one or two of fluoro, chloro, hydroxy, amino, methylamino, dimethylamino or acetyl; with the proviso that R<sub>5</sub> is not unsubstituted phenyl;

10 R<sub>11</sub> is hydrogen, hydroxy, fluoro, chloro, COO(C<sub>1</sub>-C<sub>2</sub> alkyl), cyano, or CO(C<sub>1</sub>-C<sub>2</sub> alkyl); and

R<sub>12</sub> is hydrogen or C<sub>1</sub>-C<sub>4</sub> alkyl; with the proviso that (1) when R<sub>5</sub> is 4-bromophenyl, R<sub>3</sub> is hydrogen, and R<sub>4</sub> and R<sub>6</sub> are methyl, then B is not methylamino or ethyl, and (2) when R<sub>5</sub> is 4-bromophenyl, and R<sub>3</sub>, R<sub>4</sub> and R<sub>6</sub> are methyl, then B is not 2-hydroxyethylamino.

15

4. A pharmaceutical composition according to claim 1 wherein said corticotropin releasing factor antagonist is a compound of formula



20 wherein

A is CR<sub>7</sub> or N;

B is NR<sub>1</sub>R<sub>2</sub>, CR<sub>1</sub>R<sub>2</sub>R<sub>11</sub>, C(=CR<sub>2</sub>R<sub>12</sub>)R<sub>1</sub>, NHCHR<sub>1</sub>R<sub>2</sub>, OCHR<sub>1</sub>R<sub>2</sub>, SCHR<sub>1</sub>R<sub>2</sub>, CHR<sub>2</sub>OR<sub>12</sub>, CHR<sub>2</sub>SR<sub>12</sub>, C(S)R<sub>2</sub> or C(O)R<sub>2</sub>;

G is oxygen, sulfur, NH, NH<sub>3</sub>, hydrogen, methoxy, ethoxy, trifluoromethoxy,

25 methyl, ethyl, thiomethoxy, NH<sub>2</sub>, NHCH<sub>3</sub>, N(CH<sub>3</sub>)<sub>2</sub> or trifluoromethyl;

Y is CH or N;

Z is NH, O, S, N (C<sub>1</sub>-C<sub>2</sub> alkyl), or CR<sub>13</sub>R<sub>14</sub>, wherein R<sub>13</sub> and R<sub>14</sub> are each independently hydrogen, trifluoromethyl, or C<sub>1</sub>-C<sub>4</sub> alkyl, or one of R<sub>13</sub> and R<sub>14</sub> may be cyano, chloro, bromo, iodo, fluoro, hydroxy, O(C<sub>1</sub>-C<sub>2</sub> alkyl), amino, NH(C<sub>1</sub>-C<sub>2</sub> alkyl), or CR<sub>13</sub>R<sub>14</sub> may be C=O or cyclopropyl;

R<sub>1</sub> is C<sub>1</sub>-C<sub>6</sub> alkyl which may be substituted by one or two substituents R<sub>8</sub> independently selected from the group consisting of hydroxy, fluoro, chloro, bromo, iodo, C<sub>1</sub>-C<sub>4</sub> alkoxy, O-CO-(C<sub>1</sub>-C<sub>4</sub> alkyl), O-CO-NH(C<sub>1</sub>-C<sub>4</sub> alkyl), O-CO-N(C<sub>1</sub>-C<sub>4</sub> alkyl)(C<sub>1</sub>-C<sub>2</sub> alkyl), NH(C<sub>1</sub>-C<sub>4</sub> alkyl), N(C<sub>1</sub>-C<sub>2</sub> alkyl)(C<sub>1</sub>-C<sub>4</sub> alkyl), S(C<sub>1</sub>-C<sub>4</sub> alkyl), N(C<sub>1</sub>-C<sub>4</sub> alkyl)CO(C<sub>1</sub>-C<sub>4</sub> alkyl), NHCO(C<sub>1</sub>-C<sub>4</sub> alkyl), COO(C<sub>1</sub>-C<sub>4</sub> alkyl), CONH(C<sub>1</sub>-C<sub>4</sub> alkyl), CON(C<sub>1</sub>-C<sub>4</sub> alkyl)(C<sub>1</sub>-C<sub>2</sub> alkyl), S(C<sub>1</sub>-C<sub>4</sub> alkyl), CN, NO<sub>2</sub>, SO(C<sub>1</sub>-C<sub>4</sub> alkyl), SO<sub>2</sub>(C<sub>1</sub>-C<sub>4</sub> alkyl), and said C<sub>1</sub>-C<sub>6</sub> alkyl or C<sub>1</sub>-C<sub>4</sub> alkyl may contain one double or triple bond;

R<sub>2</sub> is C<sub>1</sub>-C<sub>12</sub> alkyl, aryl or (C<sub>1</sub>-C<sub>4</sub> alkylene)aryl wherein said aryl is phenyl, naphthyl, thienyl, benzothienyl, pyridyl, quinolyl, pyrazinyl, pyrimidyl, imidazolyl, furanyl, benzofuranyl, benzothiazolyl, isothiazolyl, benzothiazolyl, benzisoxazolyl, benzimidazolyl, indolyl, or benzoxazolyl; 3- to 8-membered cycloalkyl or (C<sub>1</sub>-C<sub>6</sub> alkylene)cycloalkyl, wherein said cycloalkyl may contain one or two of O, S or N-R<sub>9</sub> wherein R<sub>9</sub> is hydrogen, or C<sub>1</sub>-C<sub>4</sub> alkyl, wherein the above defined R<sub>2</sub> may be substituted independently by from one to three of chloro, fluoro, or C<sub>1</sub>-C<sub>4</sub> alkyl, or one of bromo, iodo, C<sub>1</sub>-C<sub>6</sub> alkoxy, O-CO-(C<sub>1</sub>-C<sub>6</sub> alkyl), O-CO-N(C<sub>1</sub>-C<sub>4</sub> alkyl)(C<sub>1</sub>-C<sub>2</sub> alkyl), S(C<sub>1</sub>-C<sub>6</sub> alkyl), CN, NO<sub>2</sub>, SO(C<sub>1</sub>-C<sub>4</sub> alkyl), or SO<sub>2</sub>(C<sub>1</sub>-C<sub>4</sub> alkyl), and wherein said C<sub>1</sub>-C<sub>12</sub> alkyl or C<sub>1</sub>-C<sub>4</sub> alkylene may contain one double or triple bond; or

NR<sub>1</sub>R<sub>2</sub> or CR<sub>1</sub>R<sub>2</sub>R<sub>11</sub> may form a saturated 5- to 8-membered carbocyclic ring which may contain one or two double bonds or one or two of O or S;

R<sub>3</sub> is methyl, ethyl, fluoro, chloro, bromo, iodo, cyano, methoxy, OCF<sub>3</sub>, methylthio, methylsulfonyl, CH<sub>2</sub>OH or CH<sub>2</sub>OCH<sub>3</sub>;

R<sub>4</sub> is hydrogen, C<sub>1</sub>-C<sub>4</sub> alkyl, fluoro, chloro, bromo, iodo, C<sub>1</sub>-C<sub>4</sub> alkoxy, amino, nitro, NH(C<sub>1</sub>-C<sub>4</sub> alkyl), N(C<sub>1</sub>-C<sub>4</sub> alkyl)(C<sub>1</sub>-C<sub>2</sub> alkyl), SO<sub>n</sub>(C<sub>1</sub>-C<sub>4</sub> alkyl), wherein n is 0, 1 or 2, cyano, hydroxy, CO(C<sub>1</sub>-C<sub>4</sub> alkyl), CHO, or COO(C<sub>1</sub>-C<sub>4</sub> alkyl), wherein said C<sub>1</sub>-C<sub>4</sub> alkyl may contain one or two double or triple bonds and may be substituted by one or two of hydroxy, amino, carboxy, NHCOCH<sub>3</sub>, NH(C<sub>1</sub>-C<sub>2</sub> alkyl), N(C<sub>1</sub>-C<sub>2</sub> alkyl)<sub>2</sub>, COO(C<sub>1</sub>-C<sub>4</sub> alkyl), CO(C<sub>1</sub>-C<sub>4</sub> alkyl), C<sub>1</sub>-C<sub>3</sub> alkoxy, C<sub>1</sub>-C<sub>3</sub> thioalkyl, fluoro, chloro, cyano or nitro;

R<sub>5</sub> is phenyl, naphthyl, thienyl, benzothienyl, pyridyl, quinolyl, pyrazinyl, pyrimidyl, furanyl, benzofuranyl, benzothiazolyl, or indolyl, wherein each one of the above groups R<sub>5</sub> is substituted independently by from one to three of fluoro, chloro, C<sub>1</sub>-C<sub>6</sub> alkyl, or C<sub>1</sub>-C<sub>6</sub> alkoxy, or one of hydroxy, iodo, bromo, formyl, cyano, nitro, trifluoromethyl, amino, NH(C<sub>1</sub>-C<sub>4</sub> alkyl), N(C<sub>1</sub>-C<sub>6</sub>)(C<sub>1</sub>-C<sub>2</sub> alkyl), COOH, COO(C<sub>1</sub>-C<sub>4</sub> alkyl), CO(C<sub>1</sub>-C<sub>4</sub> alkyl), SO<sub>2</sub>NH(C<sub>1</sub>-C<sub>4</sub> alkyl), SO<sub>2</sub>N(C<sub>1</sub>-C<sub>4</sub> alkyl)(C<sub>1</sub>-C<sub>2</sub> alkyl), SO<sub>2</sub>NH<sub>2</sub>,

NHSO<sub>2</sub>(C<sub>1</sub>-C<sub>4</sub> alkyl), S(C<sub>1</sub>-C<sub>6</sub> alkyl), or SO<sub>2</sub>(C<sub>1</sub>-C<sub>6</sub> alkyl), wherein said C<sub>1</sub>-C<sub>4</sub> alkyl and C<sub>1</sub>-C<sub>6</sub> alkyl may be substituted by one or two of fluoro, hydroxy, amino, methylamino, dimethylamino or acetyl;

5 R<sub>6</sub> is hydrogen, or C<sub>1</sub>-C<sub>6</sub> alkyl, wherein said C<sub>1</sub>-C<sub>6</sub> alkyl may be substituted by one hydroxy, methoxy, ethoxy or fluoro;

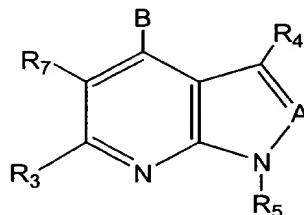
R<sub>7</sub> is hydrogen, C<sub>1</sub>-C<sub>4</sub> alkyl, fluoro, chloro, bromo, iodo, cyano, hydroxy, O(C<sub>1</sub>-C<sub>4</sub> alkyl), C(O)(C<sub>1</sub>-C<sub>4</sub> alkyl), or C(O)O(C<sub>1</sub>-C<sub>4</sub> alkyl), wherein the C<sub>1</sub>-C<sub>4</sub> alkyl groups may be substituted with one hydroxy, chloro or bromo, or one to three fluoro;

R<sub>11</sub> is hydrogen, hydroxy, fluoro, or methoxy;

10 R<sub>12</sub> is hydrogen or C<sub>1</sub>-C<sub>4</sub> alkyl; and

R<sub>16</sub> and R<sub>17</sub> are each independently hydrogen, hydroxy, methyl, ethyl, methoxy, or ethoxy, except that they are not both methoxy or ethoxy, and CR<sub>4</sub>R<sub>6</sub> and CR<sub>16</sub>R<sub>17</sub> each independently may be C=O.

15 5. A pharmaceutical composition according to claim 1 wherein said corticotropin releasing factor antagonist is a compound of formula



and the pharmaceutically acceptable acid addition salts thereof, wherein

A is N or -CR<sub>6</sub>;

20 B is -NR<sub>1</sub>R<sub>2</sub>, -CR<sub>1</sub>R<sub>2</sub>R<sub>11</sub>, -C(=CR<sub>2</sub>R<sub>12</sub>)R<sub>1</sub>, -NHCHR<sub>1</sub>R<sub>2</sub>, -OCHR<sub>1</sub>R<sub>2</sub>, -SCHR<sub>1</sub>R<sub>2</sub>, -CHR<sub>2</sub>OR<sub>12</sub>, -CHR<sub>2</sub>SR<sub>12</sub>, -C(S)R<sub>1</sub> or -C(O)R<sub>1</sub>;

R<sub>1</sub> is C<sub>1</sub>-C<sub>6</sub> alkyl which may optionally be substituted with one or two substituents independently selected from the group consisting of hydroxy, fluoro, chloro, bromo, iodo, C<sub>1</sub>-C<sub>4</sub> alkoxy, -O-CO-(C<sub>1</sub>-C<sub>4</sub> alkyl), -O-CO-NH(C<sub>1</sub>-C<sub>4</sub> alkyl), -O-CO-N(C<sub>1</sub>-C<sub>4</sub> alkyl)(C<sub>1</sub>-C<sub>2</sub> alkyl), -NH(C<sub>1</sub>-C<sub>4</sub> alkyl), -N(C<sub>1</sub>-C<sub>2</sub> alkyl)(C<sub>1</sub>-C<sub>4</sub> alkyl), -S(C<sub>1</sub>-C<sub>4</sub> alkyl), -N(C<sub>1</sub>-C<sub>4</sub> alkyl)CO(C<sub>1</sub>-C<sub>4</sub> alkyl), -NHCO(C<sub>1</sub>-C<sub>4</sub> alkyl), -COO(C<sub>1</sub>-C<sub>4</sub> alkyl), -CONH(C<sub>1</sub>-C<sub>4</sub> alkyl), -CON(C<sub>1</sub>-C<sub>4</sub> alkyl)(C<sub>1</sub>-C<sub>2</sub> alkyl), CN, NO<sub>2</sub>, -SO(C<sub>1</sub>-C<sub>4</sub> alkyl), -SO<sub>2</sub>(C<sub>1</sub>-C<sub>4</sub> alkyl), and wherein any of the foregoing C<sub>1</sub>-C<sub>4</sub> alkyl and C<sub>1</sub>-C<sub>6</sub> alkyl groups may optionally contain one carbon-carbon double or triple bond;

R<sub>2</sub> is C<sub>1</sub>-C<sub>12</sub> alkyl, aryl, -(C<sub>1</sub>-C<sub>4</sub> alkylene)aryl wherein said aryl is phenyl, naphthyl, thienyl, benzothienyl, pyridyl, quinolyl, pyrazinyl, pyrimidyl, imidazolyl, furanyl, benzofuranyl, benzothiazolyl, isothiazolyl, benzothiazolyl, thiazolyl, isoxazolyl, benzisoxazolyl, benzimidazolyl, triazolyl, pyrazolyl, pyrrolyl, indolyl, 5 oxazolyl, or benzoxazolyl; or 3- to 8- membered cycloalkyl or -(C<sub>1</sub>-C<sub>6</sub> alkylene)cycloalkyl, wherein one or two of the ring carbons of said cycloalkyl having at least 4 ring members and the cycloalkyl moiety of said -(C<sub>1</sub>-C<sub>6</sub> alkylene)cycloalkyl having at least 4 ring members may optionally be replaced by an oxygen or sulfur atom or by N-Z wherein Z is hydrogen; or C<sub>1</sub>-C<sub>4</sub> alkyl, and wherein each of said 10 groups R<sub>2</sub> may optionally be substituted with from one to three substituents independently selected from chloro, fluoro, and C<sub>1</sub>-C<sub>4</sub> alkyl, or by one substituent selected from bromo, iodo, C<sub>1</sub>-C<sub>6</sub> alkoxy, -O-CO-(C<sub>1</sub>-C<sub>6</sub> alkyl), -S(C<sub>1</sub>-C<sub>6</sub> alkyl), -COO(C<sub>1</sub>-C<sub>4</sub> alkyl), CN, NO<sub>2</sub>, -SO(C<sub>1</sub>-C<sub>4</sub> alkyl), and -SO<sub>2</sub>(C<sub>1</sub>-C<sub>4</sub> alkyl), and wherein 15 said C<sub>1</sub>-C<sub>12</sub> alkyl and the C<sub>1</sub>-C<sub>4</sub> alkylene moiety of said -(C<sub>1</sub>-C<sub>4</sub> alkylene)aryl may optionally contain one carbon-carbon double or triple bond;

or -NR<sub>1</sub>R<sub>2</sub> may form a saturated 5- to 8-membered heterocyclic ring, or -CHR<sub>1</sub>R<sub>2</sub> may form a saturated 5- to 8-membered carbocyclic ring, wherein each of these rings may optionally contain one or two carbon-carbon double bonds and wherein one or two of the carbon atoms of each of these rings may optionally be 20 replaced with a sulfur or oxygen atom;

R<sub>3</sub> is C<sub>1</sub>-C<sub>4</sub> alkyl, fluoro, chloro, bromo, iodo, -CH<sub>2</sub>OH, -CH<sub>2</sub>OCH<sub>3</sub>, -O(C<sub>1</sub>-C<sub>3</sub> alkyl), -S(C<sub>1</sub>-C<sub>3</sub> alkyl), or -SO<sub>2</sub>(C<sub>1</sub>-C<sub>3</sub> alkyl), wherein said C<sub>1</sub>-C<sub>3</sub> alkyl may optionally contain one carbon-carbon double or triple bond;

R<sub>4</sub> is hydrogen, C<sub>1</sub>-C<sub>6</sub> alkyl, fluoro, chloro, bromo, iodo, C<sub>1</sub>-C<sub>4</sub> alkoxy, amino, 25 -NHCH<sub>3</sub>, -N(CH<sub>3</sub>)<sub>2</sub>, -CH<sub>2</sub>OH, -CH<sub>2</sub>OCH<sub>3</sub>, or -SO<sub>n</sub>(C<sub>1</sub>-C<sub>4</sub> alkyl), wherein n is 0, 1 or 2, cyano, hydroxy, -CO(C<sub>1</sub>-C<sub>4</sub> alkyl), -CHO, or -COO(C<sub>1</sub>-C<sub>4</sub> alkyl) wherein the C<sub>1</sub>-C<sub>4</sub> alkyl moieties in the foregoing R<sub>4</sub> groups may optionally contain one carbon-carbon double or triple bond;

R<sub>5</sub> is phenyl, naphthyl, thienyl, benzothienyl, pyridyl, pyrimidyl, benzofuranyl, 30 pyrazinyl or benzothiazolyl, wherein each one of said groups R<sub>5</sub> may optionally be substituted with from one to three substituents independently selected from fluoro, chloro, C<sub>1</sub>-C<sub>6</sub> alkyl and C<sub>1</sub>-C<sub>6</sub> alkoxy, or by one substituent selected from iodo, hydroxy, bromo, formyl, cyano, nitro, amino, trifluoromethyl, -NH(C<sub>1</sub>-C<sub>4</sub> alkyl), -N(C<sub>1</sub>-C<sub>6</sub>)(C<sub>1</sub>-C<sub>2</sub> alkyl), -COO(C<sub>1</sub>-C<sub>4</sub> alkyl), -CO(C<sub>1</sub>-C<sub>4</sub> alkyl), -COOH, -SO<sub>2</sub>NH(C<sub>1</sub>-C<sub>4</sub> alkyl),

-SO<sub>2</sub>N(C<sub>1</sub>-C<sub>4</sub> alkyl)(C<sub>1</sub>-C<sub>2</sub> alkyl), -SO<sub>2</sub>NH<sub>2</sub>, -NHSO<sub>2</sub>(C<sub>1</sub>-C<sub>4</sub> alkyl), -S(C<sub>1</sub>-C<sub>6</sub> alkyl) and -SO<sub>2</sub>(C<sub>1</sub>-C<sub>6</sub> alkyl), wherein each of said C<sub>1</sub>-C<sub>4</sub> alkyl and C<sub>1</sub>-C<sub>6</sub> alkyl moieties in the foregoing R<sup>5</sup> groups may optionally be substituted with one to three fluorine atoms;

R<sub>6</sub> is hydrogen, C<sub>1</sub>-C<sub>4</sub> alkyl, fluoro, chloro, bromo, iodo, -CH<sub>2</sub>OH, -CH<sub>2</sub>OCH<sub>3</sub>,

5 or C<sub>1</sub>-C<sub>4</sub> alkoxy;

R<sub>7</sub> is hydrogen, C<sub>1</sub>-C<sub>4</sub> alkyl, fluoro, chloro, bromo, iodo, -O(C<sub>1</sub>-C<sub>4</sub> alkyl), cyano, -CH<sub>2</sub>OH, -CH<sub>2</sub>O(C<sub>1</sub>-C<sub>2</sub> alkyl), -CO(C<sub>1</sub>-C<sub>2</sub> alkyl), or -COO(C<sub>1</sub>-C<sub>2</sub> alkyl);

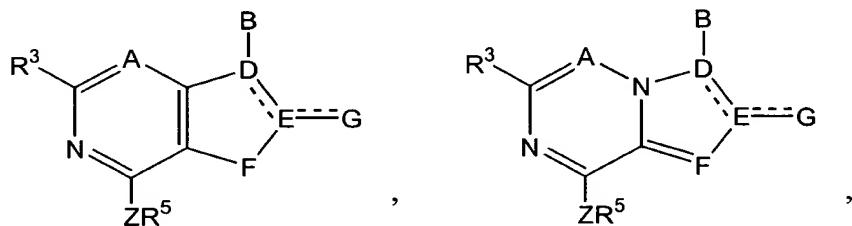
R<sub>11</sub> is hydrogen, hydroxy, fluoro, or methoxy; and

R<sub>12</sub> is hydrogen or C<sub>1</sub>-C<sub>4</sub> alkyl;

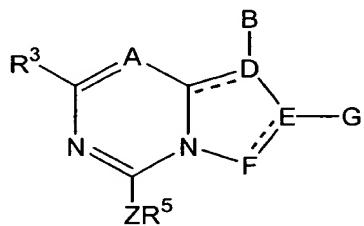
10 with the proviso that when A is N, then: (a) B is not unsubstituted alkyl; (b) R<sub>5</sub> is not unsubstituted phenyl or monosubstituted phenyl; and (c) R<sub>3</sub> is not unsubstituted alkyl;

or a pharmaceutically acceptable salt of such compound.

15 6. A pharmaceutical composition according to claim 1 wherein said corticotropin releasing factor antagonist is a compound of formula



or



or a pharmaceutically acceptable salt thereof, wherein

20 the dashed lines represent optional double bonds;

A is nitrogen or CR<sup>7</sup>;

B is -NR<sup>1</sup>R<sup>2</sup>, -CR<sup>1</sup>R<sup>2</sup>R<sup>10</sup>, -C(=CR<sup>2</sup>R<sup>11</sup>)R<sup>1</sup>, -NHCR<sup>1</sup>R<sup>2</sup>R<sup>10</sup>, -OCR<sup>1</sup>R<sup>2</sup>R<sup>10</sup>, -SCR<sup>1</sup>R<sup>2</sup>R<sup>10</sup>, -CR<sup>2</sup>R<sup>10</sup>NHR<sup>1</sup>, -CR<sup>2</sup>R<sup>10</sup>OR<sup>1</sup>, -CR<sup>2</sup>R<sup>10</sup>SR<sup>1</sup> or -COR<sup>2</sup>;

D is nitrogen and is single bonded to all atoms to which it is attached, or D is carbon and is either double bonded to E in formulas I and II or double bonded to the adjacent carbon atom common to both fused rings in formula III, or D is CH and is single bonded to E in formulas I and II;

5 E is nitrogen, CH or carbon;

F is oxygen, sulfur,  $\text{CHR}^4$  or  $\text{NR}^4$  when it is single bonded to E and F is nitrogen or  $\text{CR}^4$  when it is double bonded to E;

G, when single bonded to E, is hydrogen,  $\text{C}_1\text{-C}_4$  alkyl,  $-\text{S}(\text{C}_1\text{-C}_4$  alkyl),  $-\text{O}(\text{C}_1\text{-C}_4$  alkyl),  $\text{NH}_2$ ,  $-\text{NH}(\text{C}_1\text{-C}_4$  alkyl) or  $-\text{N}(\text{C}_1\text{-C}_2$  alkyl)( $\text{C}_1\text{-C}_4$  alkyl), wherein each of the

10  $\text{C}_1\text{-C}_4$  alkyl groups of G may optionally be substituted with one hydroxy,  $-\text{O}(\text{C}_1\text{-C}_2$  alkyl) or fluoro group; G, when double bonded to E, is oxygen, sulfur or NH; and G, when E is nitrogen and double bonded to D or F, is absent;

$\text{R}^1$  is hydrogen,  $\text{C}_1\text{-C}_6$  alkyl optionally substituted with one or two substituents  $\text{R}^8$  independently selected from hydroxy, fluoro, chloro, bromo, iodo,  $\text{C}_1\text{-C}_4$  alkoxy,

15  $\text{CF}_3$ ,  $-\text{C}(=\text{O})\text{O}(\text{C}_1\text{-C}_4)$  alkyl,  $-\text{OC}(=\text{O})(\text{C}_1\text{-C}_4$  alkyl),  $-\text{OC}(=\text{O})\text{N}(\text{C}_1\text{-C}_4$  alkyl)( $\text{C}_1\text{-C}_2$  alkyl),  $-\text{NHCO}(\text{C}_1\text{-C}_4$  alkyl),  $-\text{COOH}$ ,  $-\text{COO}(\text{C}_1\text{-C}_4$  alkyl),  $-\text{CONH}(\text{C}_1\text{-C}_4$  alkyl),  $-\text{CON}(\text{C}_1\text{-C}_4$  alkyl)( $\text{C}_1\text{-C}_2$  alkyl),  $-\text{S}(\text{C}_1\text{-C}_4$  alkyl),  $-\text{CN}$ ,  $-\text{NO}_2$ ,  $-\text{SO}(\text{C}_1\text{-C}_4$  alkyl),  $-\text{SO}_2(\text{C}_1\text{-C}_4$  alkyl),  $-\text{SO}_2\text{NH}(\text{C}_1\text{-C}_4$  alkyl) and  $-\text{SO}_2\text{N}(\text{C}_1\text{-C}_4$  alkyl)( $\text{C}_1\text{-C}_2$  alkyl), wherein each of the  $\text{C}_1\text{-C}_4$  alkyl groups in the foregoing  $\text{R}^1$  groups may optionally contain one or two double or

20 triple bonds;

$\text{R}^2$  is  $\text{C}_1\text{-C}_{12}$  alkyl which may optionally contain from one to three double or triple bonds, aryl or  $(\text{C}_1\text{-C}_4$  alkylene)aryl, wherein said aryl and the aryl moiety of said  $(\text{C}_1\text{-C}_4$  alkylene)aryl is selected from phenyl, naphthyl, thiienyl, benzothienyl, pyridyl, quinolyl, pyrazinyl, pyrimidinyl, imidazolyl, furanyl, benzofuranyl, benzothiazolyl,

25 isothiazolyl, pyrazolyl, pyrrolyl, indolyl, pyrrolopyridyl, oxazolyl and benzoxazolyl;  $\text{C}_3\text{-C}_8$  cycloalkyl or  $(\text{C}_1\text{-C}_6$  alkylene)( $\text{C}_3\text{-C}_8$  cycloalkyl), wherein one or two of the carbon atoms of said cycloalkyl and the 5 to 8 membered cycloalkyl moieties of said  $(\text{C}_1\text{-C}_6$  alkylene)( $\text{C}_3\text{-C}_8$  cycloalkyl) may optionally and independently be replaced by an oxygen or sulfur atom or by  $\text{NZ}^2$  wherein  $Z^2$  is selected from hydrogen,  $\text{C}_1\text{-C}_4$  alkyl,

30 benzyl and  $\text{C}_1\text{-C}_4$  alkanoyl, and wherein each of the foregoing  $\text{R}^2$  groups may optionally be substituted with from one to three substituents independently selected from chloro, fluoro, hydroxy and  $\text{C}_1\text{-C}_4$  alkyl, or with one substituent selected from bromo, iodo,  $\text{C}_1\text{-C}_6$  alkoxy,  $-\text{OC}(=\text{O})(\text{C}_1\text{-C}_6$  alkyl),  $-\text{OC}(=\text{O})\text{N}(\text{C}_1\text{-C}_4$  alkyl)( $\text{C}_1\text{-C}_2$  alkyl),  $-\text{S}(\text{C}_1\text{-C}_6$  alkyl), amino,  $-\text{NH}(\text{C}_1\text{-C}_2$  alkyl),  $-\text{N}(\text{C}_1\text{-C}_2$  alkyl)( $\text{C}_1\text{-C}_4$  alkyl),  $-\text{N}(\text{C}_1\text{-C}_4$  alkyl)-

CO-(C<sub>1</sub>-C<sub>4</sub> alkyl), -NHCO(C<sub>1</sub>-C<sub>4</sub> alkyl), -COOH, -COO(C<sub>1</sub>-C<sub>4</sub> alkyl), -CONH(C<sub>1</sub>-C<sub>4</sub> alkyl), -CON(C<sub>1</sub>-C<sub>4</sub> alkyl)(C<sub>1</sub>-C<sub>2</sub> alkyl), -SH, -CN, -NO<sub>2</sub>, -SO(C<sub>1</sub>-C<sub>4</sub> alkyl), -SO<sub>2</sub>(C<sub>1</sub>-C<sub>4</sub> alkyl), -SO<sub>2</sub>NH(C<sub>1</sub>-C<sub>4</sub> alkyl) and -SO<sub>2</sub>N(C<sub>1</sub>-C<sub>4</sub> alkyl)(C<sub>1</sub>-C<sub>2</sub> alkyl);

-NR<sup>1</sup>R<sup>2</sup> or CR<sup>1</sup>R<sup>2</sup>R<sup>10</sup> may form a saturated 3 to 8 membered carbocyclic ring

5 which may optionally contain from one to three double bonds and wherein one or two of the ring carbon atoms of such 5 to 8 membered rings may optionally and independently be replaced by an oxygen or sulfur atom or by NZ<sup>3</sup> wherein Z<sup>3</sup> is hydrogen, C<sub>1</sub>-C<sub>4</sub> alkyl, benzyl or C<sub>1</sub>-C<sub>4</sub> alkanoyl;

10 R<sup>3</sup> is hydrogen, C<sub>1</sub>-C<sub>4</sub> alkyl, -O(C<sub>1</sub>-C<sub>4</sub> alkyl), chloro, fluoro, bromo, iodo, -CN, -S(C<sub>1</sub>-C<sub>4</sub> alkyl) or -SO<sub>2</sub>(C<sub>1</sub>-C<sub>4</sub> alkyl) wherein each of the (C<sub>1</sub>-C<sub>4</sub> alkyl) moieties in the foregoing R<sup>3</sup> groups may optionally be substituted with one substituent R<sup>9</sup> selected from hydroxy, fluoro and (C<sub>1</sub>-C<sub>2</sub> alkoxy);

15 each R<sup>4</sup> is, independently, hydrogen, (C<sub>1</sub>-C<sub>6</sub> alkyl), fluoro, chloro, bromo, iodo, hydroxy, cyano, amino, nitro, -O(C<sub>1</sub>-C<sub>4</sub> alkyl), -N(C<sub>1</sub>-C<sub>4</sub> alkyl)(C<sub>1</sub>-C<sub>2</sub> alkyl), -S(C<sub>1</sub>-C<sub>4</sub> alkyl), -SO(C<sub>1</sub>-C<sub>4</sub> alkyl), -SO<sub>2</sub>(C<sub>1</sub>-C<sub>4</sub>)alkyl, -CO(C<sub>1</sub>-C<sub>4</sub> alkyl), -C(=O)H or -C(=O)O(C<sub>1</sub>-C<sub>4</sub> alkyl), wherein each of the (C<sub>1</sub>-C<sub>6</sub> alkyl) and (C<sub>1</sub>-C<sub>4</sub> alkyl) moieties in the foregoing R<sup>4</sup> groups may optionally contain one or two double or triple bonds and may optionally be substituted with one or two substituents independently selected from hydroxy, amino, C<sub>1</sub>-C<sub>3</sub> alkoxy, dimethylamino, methylamino, ethylamino,

20 -NHC(=O)CH<sub>3</sub>, fluoro, chloro, C<sub>1</sub>-C<sub>3</sub> thioalkyl, -CN, -COOH, -C(=O)O(C<sub>1</sub>-C<sub>4</sub> alkyl), -C(=O)(C<sub>1</sub>-C<sub>4</sub> alkyl) and -NO<sub>2</sub>;

25 R<sup>5</sup> is phenyl, naphthyl, thienyl, benzothienyl, pyridyl, quinolyl, pyrazinyl, furanyl, benzofuranyl, benzothiazolyl, benzisothiazolyl, benzisoxazolyl, benzimidazolyl, indolyl, benzoxazolyl or C<sub>3</sub>-C<sub>8</sub> cycloalkyl wherein one or two of the carbon atoms of said cycloalkyl rings that contain at least 5 ring members may optionally and independently be replaced by an oxygen or sulfur atom or by NZ<sup>4</sup> wherein Z<sup>4</sup> is hydrogen, C<sub>1</sub>-C<sub>4</sub> alkyl or benzyl; and wherein each of the foregoing R<sup>5</sup> groups is substituted with from one to four substituents R<sup>12</sup> wherein one to three of said substituents may be selected, independently, from chloro, C<sub>1</sub>-C<sub>6</sub> alkyl and -O(C<sub>1</sub>-C<sub>6</sub> alkyl) and one of said substituents may be selected from bromo, iodo, formyl, -CN, -CF<sub>3</sub>, -NO<sub>2</sub>, -NH<sub>2</sub>, -NH(C<sub>1</sub>-C<sub>4</sub> alkyl), -N(C<sub>1</sub>-C<sub>2</sub> alkyl)(C<sub>1</sub>-C<sub>6</sub> alkyl), -C(=O)O(C<sub>1</sub>-C<sub>4</sub> alkyl), -C(=O)(C<sub>1</sub>-C<sub>4</sub> alkyl), -COOH, -SO<sub>2</sub>NH(C<sub>1</sub>-C<sub>4</sub> alkyl), -SO<sub>2</sub>N(C<sub>1</sub>-C<sub>2</sub> alkyl)(C<sub>1</sub>-C<sub>4</sub> alkyl), -SO<sub>2</sub>NH<sub>2</sub>, -NHSO<sub>2</sub>(C<sub>1</sub>-C<sub>4</sub> alkyl), -S(C<sub>1</sub>-C<sub>6</sub> alkyl) and -SO<sub>2</sub>(C<sub>1</sub>-C<sub>6</sub> alkyl), and wherein each of the C<sub>1</sub>-C<sub>4</sub> alkyl and C<sub>1</sub>-C<sub>6</sub> alkyl moieties in the foregoing R<sup>5</sup> groups may

optionally be substituted with one or two substituents independently selected from fluoro, hydroxy, amino, methylamino, dimethylamino and acetyl;

R<sup>7</sup> is hydrogen, C<sub>1</sub>-C<sub>4</sub> alkyl, halo, cyano, hydroxy, -O(C<sub>1</sub>-C<sub>4</sub> alkyl) -C(=O)(C<sub>1</sub>-C<sub>4</sub> alkyl), -C(=O)O(C<sub>1</sub>-C<sub>4</sub> alkyl), -OCF<sub>3</sub>, -CF<sub>3</sub>, -CH<sub>2</sub>OH, -CH<sub>2</sub>O(C<sub>1</sub>-C<sub>4</sub> alkyl);

5 R<sup>10</sup> is hydrogen, hydroxy, methoxy or fluoro;

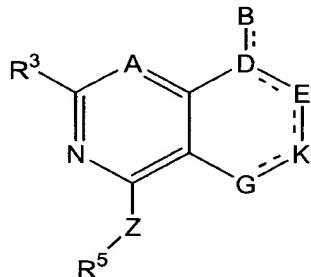
R<sup>11</sup> is hydrogen or C<sub>1</sub>-C<sub>4</sub> alkyl; and

Z is NH, oxygen, sulfur, -N(C<sub>1</sub>-C<sub>4</sub> alkyl), -NC(=O)(C<sub>1</sub>-C<sub>2</sub> alkyl), NC(=O)O(C<sub>1</sub>-C<sub>2</sub> alkyl) or CR<sup>13</sup>R<sup>14</sup> wherein R<sup>13</sup> and R<sup>14</sup> are independently selected from hydrogen, trifluoromethyl and methyl with the exception that one of R<sup>13</sup> and R<sup>14</sup> can be cyano;

10 with the proviso that: (a) in the five membered rings of structures I, II and III, there can not be two double bonds adjacent to each other; and (b) when R<sup>4</sup> is attached to nitrogen, it is not halo, cyano or nitro;

or a pharmaceutically acceptable salt of such compound.

15 7. A pharmaceutical composition according to claim 1 wherein said corticotropin releasing factor antagonist is a compound of formula



wherein the dashed lines represent optional double bonds;

A is nitrogen or CR<sup>7</sup>;

20 B is -NR<sup>1</sup>R<sup>2</sup>, -CR<sup>1</sup>R<sup>2</sup>R<sup>10</sup>, -C(=CR<sup>2</sup>R<sup>11</sup>)R<sup>1</sup>, -NHCR<sup>1</sup>R<sup>2</sup>R<sup>10</sup>, -OCR<sup>1</sup>R<sup>2</sup>R<sup>10</sup>, -SCR<sup>1</sup>R<sup>2</sup>R<sup>10</sup>, -CR<sup>2</sup>R<sup>10</sup>NHR<sup>1</sup>, -CR<sup>2</sup>R<sup>10</sup>OR<sup>1</sup>, -CR<sup>2</sup>R<sup>10</sup>SR<sup>1</sup> or -COR<sup>2</sup>, and is single bonded to D; or B is -CR<sup>1</sup>R<sup>2</sup>, and is double bonded to D and D is carbon;

D is nitrogen or CR<sup>4</sup> and is single bonded to all atoms to which it is attached, or D is carbon and is double bonded to E or double bonded to B;

25 E is oxygen, nitrogen, sulfur, C=O, C=S, CR<sup>6</sup>R<sup>12</sup>, NR<sup>6</sup> or CR<sup>6</sup>; or E is a two atom spacer, wherein one of the atoms is oxygen, nitrogen, sulfur, C=O, C=S, CR<sup>6</sup>R<sup>12</sup>, NR<sup>6</sup> or CR<sup>6</sup>, and the other is CR<sup>6</sup>R<sup>12</sup> or CR<sup>9</sup>;

K and G are each, independently, C=O, C=S, sulfur, oxygen, CHR<sup>8</sup> or NR<sup>8</sup> when single bonded to both adjacent ring atoms, or nitrogen or CR<sup>8</sup> when it is double bonded to an adjacent ring atom;

the 6- or 7-membered ring that contains D, E, K and G may contain from one to three double bonds, from zero to two heteroatoms selected from oxygen, nitrogen and sulfur, and from zero to two C=O or C=S groups, wherein the carbon atoms of such groups are part of the ring and the oxygen and sulfur atoms are substituents on the ring;

R<sup>1</sup> is C<sub>1</sub>-C<sub>6</sub> alkyl optionally substituted with from one or two substituents

10 independently selected from hydroxy, fluoro, chloro, bromo, iodo, C<sub>1</sub>-C<sub>4</sub> alkoxy, CF<sub>3</sub>, -C(=O)(C<sub>1</sub>-C<sub>4</sub> alkyl), -C(=O)-O-(C<sub>1</sub>-C<sub>4</sub>)alkyl, -OC(=O)(C<sub>1</sub>-C<sub>4</sub> alkyl), -OC(=O)N(C<sub>1</sub>-C<sub>4</sub> alkyl)(C<sub>1</sub>-C<sub>2</sub> alkyl), -NHCO(C<sub>1</sub>-C<sub>4</sub> alkyl), -COOH, -COO(C<sub>1</sub>-C<sub>4</sub> alkyl), -CONH(C<sub>1</sub>-C<sub>4</sub> alkyl), -CON(C<sub>1</sub>-C<sub>4</sub> alkyl)(C<sub>1</sub>-C<sub>2</sub> alkyl), -S(C<sub>1</sub>-C<sub>4</sub> alkyl), -CN, -NO<sub>2</sub>, -SO(C<sub>1</sub>-C<sub>4</sub> alkyl), -SO<sub>2</sub>(C<sub>1</sub>-C<sub>4</sub> alkyl), -SO<sub>2</sub>NH(C<sub>1</sub>-C<sub>4</sub> alkyl) and -SO<sub>2</sub>N(C<sub>1</sub>-C<sub>4</sub> alkyl)(C<sub>1</sub>-C<sub>2</sub> alkyl), wherein

15 each of the C<sub>1</sub>-C<sub>4</sub> alkyl groups in the foregoing R<sup>1</sup> groups may optionally contain one or two double or triple bonds;

R<sup>2</sup> is C<sub>1</sub>-C<sub>12</sub> alkyl which may optionally contain from one to three double or triple bonds, aryl or (C<sub>1</sub>-C<sub>4</sub> alkylene)aryl, wherein said aryl and the aryl moiety of said (C<sub>1</sub>-C<sub>4</sub> alkylene)aryl is selected from phenyl, naphthyl, thiienyl, benzothienyl, pyridyl, quinolyl, pyrazinyl, pyrimidinyl, imidazolyl, furanyl, benzofuranyl, benzothiazolyl, isothiazolyl, pyrazolyl, pyrrolyl, indolyl, pyrrolopyridyl, oxazolyl and benzoxazolyl; C<sub>3</sub>-C<sub>8</sub> cycloalkyl or (C<sub>1</sub>-C<sub>6</sub> alkylene)(C<sub>3</sub>-C<sub>8</sub> cycloalkyl), wherein one or two of the carbon atoms of said cycloalkyl and the 5 to 8 membered cycloalkyl moieties of said (C<sub>1</sub>-C<sub>6</sub> alkylene)(C<sub>3</sub>-C<sub>8</sub> cycloalkyl) may optionally and independently be replaced by an oxygen or sulfur and wherein each of the foregoing R<sup>2</sup> groups may optionally be substituted with from one to three substituents independently selected from chloro, fluoro, hydroxy and C<sub>1</sub>-C<sub>4</sub> alkyl, or with one substituent selected from C<sub>1</sub>-C<sub>6</sub> alkoxy, -OC(=O)(C<sub>1</sub>-C<sub>6</sub> alkyl), -OC(=O)N(C<sub>1</sub>-C<sub>4</sub> alkyl)(C<sub>1</sub>-C<sub>2</sub> alkyl), -S(C<sub>1</sub>-C<sub>6</sub> alkyl), amino, -NH(C<sub>1</sub>-C<sub>2</sub> alkyl), -N(C<sub>1</sub>-C<sub>2</sub> alkyl)(C<sub>1</sub>-C<sub>4</sub> alkyl), -N(C<sub>1</sub>-C<sub>4</sub> alkyl)-CO-(C<sub>1</sub>-C<sub>4</sub> alkyl), -NHCO(C<sub>1</sub>-C<sub>4</sub> alkyl), -COOH, -COO(C<sub>1</sub>-C<sub>4</sub> alkyl), -CONH(C<sub>1</sub>-C<sub>4</sub> alkyl), -CON(C<sub>1</sub>-C<sub>4</sub> alkyl)(C<sub>1</sub>-C<sub>2</sub> alkyl), -SH, -CN, -NO<sub>2</sub>, -SO(C<sub>1</sub>-C<sub>4</sub> alkyl), -SO<sub>2</sub>(C<sub>1</sub>-C<sub>4</sub> alkyl), -SO<sub>2</sub>NH(C<sub>1</sub>-C<sub>4</sub> alkyl) and -SO<sub>2</sub>N(C<sub>1</sub>-C<sub>4</sub> alkyl)(C<sub>1</sub>-C<sub>2</sub> alkyl);

-NR<sup>1</sup>R<sup>2</sup> or CR<sup>1</sup>R<sup>2</sup>R<sup>10</sup> may form a ring selected from saturated 3 to 8 membered rings, the 5 to 8 membered rings of which may optionally contain one or

two double bonds, and wherein one or two of the ring carbon atoms of such 5 to 8 membered rings may optionally and independently be replaced by an oxygen or sulfur atom or by NZ<sup>3</sup> wherein Z<sup>3</sup> is hydrogen or C<sub>1</sub>-C<sub>4</sub> alkyl;

R<sup>3</sup> is hydrogen, C<sub>1</sub>-C<sub>4</sub> alkyl, -O(C<sub>1</sub>-C<sub>4</sub> alkyl), chloro, fluoro, bromo, iodo,

5 -S(C<sub>1</sub>-C<sub>4</sub> alkyl) or -SO<sub>2</sub>(C<sub>1</sub>-C<sub>4</sub> alkyl);

R<sup>4</sup> is hydrogen, C<sub>1</sub>-C<sub>2</sub> alkyl, hydroxy or fluoro;

each R<sup>6</sup>, R<sup>8</sup> and R<sup>9</sup> that is attached to a carbon atom is selected, independently, from hydrogen, C<sub>1</sub>-C<sub>2</sub> alkyl, fluoro, chloro, bromo, iodo, hydroxy, hydroxymethyl, formyl, trifluoromethyl, cyano, amino, nitro, -O(C<sub>1</sub>-C<sub>2</sub> alkyl), -N(C<sub>1</sub>-C<sub>2</sub> alkyl)(C<sub>1</sub>-C<sub>2</sub> alkyl), -S(C<sub>1</sub>-C<sub>2</sub> alkyl), -CO(C<sub>1</sub>-C<sub>2</sub> alkyl), -C(=O)H or -C(=O)O(C<sub>1</sub>-C<sub>2</sub> alkyl), 10 wherein each of the C<sub>1</sub>-C<sub>2</sub> alkyl moieties in the foregoing R<sup>6</sup>, R<sup>8</sup>, and R<sup>9</sup> groups may optionally contain one double or triple bond; and each R<sup>6</sup>, R<sup>8</sup>, and R<sup>9</sup> that is attached to a nitrogen atom is selected, independently, from hydrogen and C<sub>1</sub>-C<sub>4</sub> alkyl;

R<sup>5</sup> is substituted phenyl, naphthyl, pyridyl or pyrimidyl, wherein each of the

15 foregoing R<sup>5</sup> groups is substituted with from two to four substituents R<sup>15</sup>, wherein from one to three of said substituents may be selected, independently, from chloro, C<sub>1</sub>-C<sub>6</sub> alkyl, -O(C<sub>1</sub>-C<sub>6</sub> alkyl) and -(C<sub>1</sub>-C<sub>6</sub> alkylene)O(C<sub>1</sub>-C<sub>6</sub> alkyl), and wherein one of said substituents may be selected, independently, from bromo, iodo, formyl, cyano, trifluoromethyl, nitro, amino, -NH(C<sub>1</sub>-C<sub>4</sub> alkyl), -N(C<sub>1</sub>-C<sub>2</sub> alkyl)(C<sub>1</sub>-C<sub>6</sub> alkyl),

20 -C(=O)O(C<sub>1</sub>-C<sub>4</sub> alkyl), -C(=O)(C<sub>1</sub>-C<sub>4</sub> alkyl), -COOH, -SO<sub>2</sub>NH(C<sub>1</sub>-C<sub>4</sub> alkyl), -SO<sub>2</sub>N(C<sub>1</sub>-C<sub>2</sub> alkyl)(C<sub>1</sub>-C<sub>4</sub> alkyl), -SO<sub>2</sub>NH<sub>2</sub>, -HSO<sub>2</sub>(C<sub>1</sub>-C<sub>4</sub> alkyl), -S(C<sub>1</sub>-C<sub>6</sub> alkyl) and -SO<sub>2</sub>(C<sub>1</sub>-C<sub>6</sub> alkyl), and wherein each of the C<sub>1</sub>-C<sub>4</sub> alkyl and C<sub>1</sub>-C<sub>6</sub> alkyl moieties in the foregoing R<sup>5</sup> groups may optionally be substituted with one or two substituents independently selected from fluoro, hydroxy, amino, methylamino, dimethylamino and

25 acetyl;

R<sup>7</sup> is hydrogen, methyl, halo, hydroxy, methoxy, -C(=O)(C<sub>1</sub>-C<sub>2</sub> alkyl), -C(=O)O(C<sub>1</sub>-C<sub>2</sub> alkyl), trifluoromethoxy, hydroxymethyl, trifluoromethyl or formyl;

R<sup>10</sup> is hydrogen, hydroxy, methoxy or fluoro;

R<sup>11</sup> is hydrogen or C<sub>1</sub>-C<sub>4</sub> alkyl;

30 R<sup>12</sup> is hydrogen or methyl; and

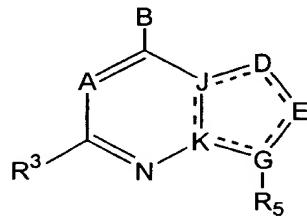
Z is NH, oxygen, sulfur, -N(C<sub>1</sub>-C<sub>4</sub> alkyl), or CR<sup>13</sup>R<sup>14</sup> wherein R<sup>13</sup> and R<sup>14</sup> are independently selected from hydrogen, and methyl with the exception that one of R<sup>13</sup> and R<sup>14</sup> may optionally be cyano;

with the proviso that: (a) in the six or seven membered rings of structures in formula I, there can not be two double bonds adjacent to each other; and (b) when D is carbon and is double bonded to B, then B is  $CR^1R^2$ ;

or a pharmaceutically acceptable salt of such compound.

5

8. A pharmaceutical composition according to claim 1 wherein said corticotropin releasing factor antagonist is a compound of formula



10 or a pharmaceutically acceptable salt thereof, wherein  
the dashed lines represent optional double bonds;  
A is nitrogen or  $CR^7$ ;  
B is  $-NR^1R^2$ ,  $-CR^1R^2R^{10}$ ,  $-C(=CR^2R^{11})R^1$ ,  $-NHCR^1R^2R^{10}$ ,  $-OCR^1R^2R^{10}$ ,  
 $-SCR^1R^2R^{10}$ ,  $-CR^2R^{10}NHR^1$ ,  $-CR^2R^{10}OR^1$ ,  $-CR^2R^{10}SR^1$  or  $-COR^2$ ;  
J and K are each independently nitrogen or carbon and both J and K are not  
15 nitrogens;  
D and E are each selected, independently, from nitrogen,  $CR^4$ ,  $C=O$ ,  $C=S$ ,  
sulfur, oxygen,  $CR^4R^6$  and  $NR^8$ ;  
G is nitrogen or carbon;  
the ring containing D, E, G, K, and J in formula I may be a saturated or  
20 unsaturated 5-membered ring and may optionally contain one or two double bonds  
and may optionally contain from one to three heteroatoms in the ring and may  
optionally have one or two  $C=O$  or  $C=S$  groups;  
R<sup>1</sup> is  $C_1-C_6$  alkyl optionally substituted with one or two substituents  
independently selected from hydroxy, fluoro, chloro, bromo, iodo,  $-O-(C_1-C_4$  alkyl),  
25  $CF_3$ ,  $-C(=O)O-(C_1-C_4$  alkyl),  $-OC(=O)(C_1-C_4$  alkyl),  $-OC(=O)N(C_1-C_4$  alkyl)( $C_1-C_2$  alkyl),  
 $-NHCO(C_1-C_4$  alkyl),  $-COOH$ ,  $-COO(C_1-C_4$  alkyl),  $-CONH(C_1-C_4$  alkyl),  $-CON(C_1-C_4$   
alkyl)( $C_1-C_2$  alkyl),  $-S(C_1-C_4$  alkyl),  $-CN$ ,  $-NO_2$ ,  $-SO(C_1-C_4$  alkyl),  $-SO_2(C_1-C_4$  alkyl),  
 $-SO_2NH(C_1-C_4$  alkyl) and  $-SO_2N(C_1-C_4$  alkyl)( $C_1-C_2$  alkyl), wherein each of the  $C_1-C_4$   
alkyl groups in the foregoing R<sup>1</sup> groups may optionally contain one or two double or  
30 triple bonds;

$R^2$  is  $C_1$ - $C_{12}$  alkyl which may optionally contain from one to three double or triple bonds, aryl or ( $C_1$ - $C_4$  alkylene)aryl, wherein said aryl and the aryl moiety of said ( $C_1$ - $C_4$  alkylene)aryl is selected from phenyl, naphthyl, thiienyl, benzothienyl, pyridyl, quinolyl, pyrazinyl, pyrimidinyl, imidazolyl, furanyl, benzofuranyl, benzothiazolyl, 5 isothiazolyl, pyrazolyl, pyrrolyl, indolyl, pyrrolopyridyl, oxazolyl and benzoxazolyl;  $C_3$ - $C_8$  cycloalkyl or ( $C_1$ - $C_6$  alkylene)( $C_3$ - $C_8$  cycloalkyl), wherein one or two of the carbon atoms of said cycloalkyl and the 5 to 8 membered cycloalkyl moieties of said ( $C_1$ - $C_6$  alkylene)( $C_3$ - $C_8$  cycloalkyl) may optionally and independently be replaced by an oxygen or sulfur atom or by  $NZ^2$  wherein  $Z^2$  is selected from hydrogen,  $C_1$ - $C_4$  alkyl, 10 benzyl and  $C_1$ - $C_4$  alkanoyl, and wherein each of the foregoing  $R^2$  groups may optionally be substituted with from one to three substituents independently selected from chloro, fluoro, hydroxy and  $C_1$ - $C_4$  alkyl, or with one substituent selected from bromo, iodo,  $C_1$ - $C_6$  alkoxy,  $-OC(=O)(C_1$ - $C_6$  alkyl),  $-OC(=O)N(C_1$ - $C_4$  alkyl)( $C_1$ - $C_2$  alkyl),  $-S(C_1$ - $C_6$  alkyl), amino,  $-NH(C_1$ - $C_2$  alkyl),  $-N(C_1$ - $C_2$  alkyl)( $C_1$ - $C_4$  alkyl),  $-N(C_1$ - $C_4$  15 alkyl)- $CO-(C_1$ - $C_4$  alkyl),  $-NHCO(C_1$ - $C_4$  alkyl),  $-COOH$ ,  $-COO(C_1$ - $C_4$  alkyl),  $-CONH(C_1$ - $C_4$  alkyl),  $-CON(C_1$ - $C_4$  alkyl)( $C_1$ - $C_2$  alkyl),  $-SH$ ,  $-CN$ ,  $-NO_2$ ,  $-SO(C_1$ - $C_4$  alkyl),  $-SO_2(C_1$ - $C_4$  alkyl),  $-SO_2NH(C_1$ - $C_4$  alkyl) and  $-SO_2N(C_1$ - $C_4$  alkyl)( $C_1$ - $C_2$  alkyl);  $-NR^1R^2$  or  $CR^1R^2R^{10}$  may form a saturated 3 to 8 membered carbocyclic ring which may optionally contain from one to three double bonds and wherein one or two 20 of the ring carbon atoms of such 5 to 8 membered rings may optionally and independently be replaced by an oxygen or sulfur atom or by  $NZ^3$  wherein  $Z^3$  is hydrogen,  $C_1$ - $C_4$  alkyl, benzyl or  $C_1$ - $C_4$  alkanoyl;

$R^3$  is hydrogen,  $C_1$ - $C_4$  alkyl,  $-O(C_1$ - $C_4$  alkyl), chloro, fluoro, bromo, iodo, ( $C_1$ - $C_2$  alkylene)- $O-(C_1$ - $C_2$  alkyl), ( $C_1$ - $C_2$  alkylene)- $OH$ , or  $-S(C_1$ - $C_4$  alkyl); 25 each  $R^4$  is, independently, hydrogen, ( $C_1$ - $C_6$  alkyl), fluoro, chloro, bromo, iodo, hydroxy, cyano, amino, ( $C_1$ - $C_2$  alkylene)- $OH$ ,  $CF_3$ ,  $CH_2SCH_3$ , nitro,  $-O(C_1$ - $C_4$  alkyl),  $-N(C_1$ - $C_4$  alkyl)( $C_1$ - $C_2$  alkyl),  $-S(C_1$ - $C_4$  alkyl),  $-CO(C_1$ - $C_4$  alkyl),  $-C(=O)H$  or  $-C(=O)O(C_1$ - $C_4$  alkyl);  $R^6$  is hydrogen, methyl or ethyl; 30  $R^8$  is hydrogen or  $C_1$ - $C_4$  alkyl;  $R^5$  is phenyl, pyridyl, pyrazinyl, pyrimidyl, pyridazinyl and wherein each of the foregoing  $R^5$  groups is substituted with from one to four substituents  $R^{13}$  wherein one to three of said substituents may be selected, independently, from fluoro, chloro,  $C_1$ - $C_6$  alkyl and  $-O(C_1$ - $C_6$  alkyl) and one of said substituents may be selected from

bromo, iodo, formyl, OH, (C<sub>1</sub>-C<sub>4</sub> alkylene)-OH, (C<sub>1</sub>-C<sub>4</sub> alkylene)-O-(C<sub>1</sub>-C<sub>2</sub> alkyl), -CN, -CF<sub>3</sub>, -NO<sub>2</sub>, -NH<sub>2</sub>, -NH(C<sub>1</sub>-C<sub>4</sub> alkyl), -N(C<sub>1</sub>-C<sub>2</sub> alkyl)(C<sub>1</sub>-C<sub>6</sub> alkyl), -OCO(C<sub>1</sub>-C<sub>4</sub> alkyl), (C<sub>1</sub>-C<sub>4</sub> alkylene)-O-(C<sub>1</sub>-C<sub>4</sub> alkyl), -S(C<sub>1</sub>-C<sub>6</sub> alkyl), (C<sub>1</sub>-C<sub>4</sub> alkylene)-S-(C<sub>1</sub>-C<sub>4</sub> alkyl), -C(=O)O(C<sub>1</sub>-C<sub>4</sub> alkyl), -C(=O)(C<sub>1</sub>-C<sub>4</sub> alkyl), -COOH, -SO<sub>2</sub>NH(C<sub>1</sub>-C<sub>4</sub> alkyl),

5 -SO<sub>2</sub>N(C<sub>1</sub>-C<sub>2</sub> alkyl)(C<sub>1</sub>-C<sub>4</sub> alkyl), -SO<sub>2</sub>NH<sub>2</sub>, -NHSO<sub>2</sub>(C<sub>1</sub>-C<sub>4</sub> alkyl), -S(C<sub>1</sub>-C<sub>6</sub> alkyl) and -SO<sub>2</sub>(C<sub>1</sub>-C<sub>6</sub> alkyl), and wherein each of the C<sub>1</sub>-C<sub>4</sub> alkyl and C<sub>1</sub>-C<sub>6</sub> alkyl moieties in the foregoing R<sup>5</sup> groups may optionally have one or two double bonds;

R<sup>7</sup> is hydrogen, C<sub>1</sub>-C<sub>4</sub> alkyl, halo (e.g., chloro, fluoro, iodo or bromo), hydroxy, -O(C<sub>1</sub>-C<sub>4</sub> alkyl), -C(=O)(C<sub>1</sub>-C<sub>4</sub> alkyl), -C(=O)O(C<sub>1</sub>-C<sub>4</sub> alkyl), -OCF<sub>3</sub>, -CF<sub>3</sub>, -CH<sub>2</sub>OH or

10 -CH<sub>2</sub>O(C<sub>1</sub>-C<sub>2</sub> alkyl);

R<sup>10</sup> is hydrogen, hydroxy, methoxy or fluoro;

R<sup>11</sup> is hydrogen or C<sub>1</sub>-C<sub>4</sub> alkyl; and

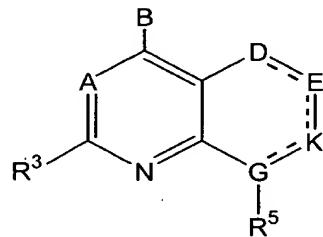
with the proviso that: a) when both J and K are carbons and D is CR<sup>4</sup> and E is nitrogen, then G can not be nitrogen; (b) when both J and K are carbons and D and

15 G are nitrogens, then E can not be CR<sup>4</sup> or C=O or C=S; (c) when both J and K are carbons and D and E are carbons, then G can not be nitrogen; (d) when G is carbon, it must be double banded to E; and (e) in the ring containing J, K, D, E and G, there can not be two double bonds adjacent to each other;

and the pharmaceutically acceptable salts of such compounds.

20

9. A pharmaceutical composition according to claim 1 wherein said corticotropin releasing factor antagonist is a compound of formula



wherein the dashed lines represent optional double bonds;

25 A is nitrogen or CR<sup>7</sup>;

B is -NR<sup>1</sup>R<sup>2</sup>, -CR<sup>1</sup>R<sup>2</sup>R<sup>10</sup>, -C(=CR<sup>2</sup>R<sup>11</sup>)R<sup>1</sup>, -NHCR<sup>1</sup>R<sup>2</sup>R<sup>10</sup>, -OCR<sup>1</sup>R<sup>2</sup>R<sup>10</sup>, -SCR<sup>1</sup>R<sup>2</sup>R<sup>10</sup>, -CR<sup>2</sup>R<sup>10</sup>NHR<sup>1</sup>, -CR<sup>2</sup>R<sup>10</sup>OR<sup>1</sup>, -CR<sup>2</sup>R<sup>10</sup>SR<sup>1</sup> or -COR<sup>2</sup>;

G is nitrogen or CR<sup>4</sup> and is single bonded to all atoms to which it is attached, or G is carbon and is double bonded to K;

K is nitrogen or CR<sup>6</sup> when double bonded to G or E, or K is oxygen, sulfur, C=O, C=S, CR<sup>6</sup>R<sup>12</sup> or NR<sup>8</sup> when single bonded to both adjacent ring atoms, or K is a two atom spacer, wherein one of the two ring atoms of the spacer is oxygen, nitrogen, sulfur, C=O, C=S, CR<sup>6</sup>R<sup>12</sup>, NR<sup>6</sup> or CR<sup>6</sup>, and the other is CR<sup>6</sup>R<sup>12</sup> or CR<sup>9</sup>;

5 D and E are each, independently, C=O, C=S, sulfur, oxygen, CR<sup>4</sup>R<sup>6</sup> or NR<sup>8</sup> when single bonded to both adjacent ring atoms, or nitrogen or CR<sup>4</sup> when it is double bonded to an adjacent ring atom;

10 the 6- or 7-membered ring that contains D, E, K and G may contain from one and sulfur, and from zero to two C=O or C=S groups, wherein the carbon atoms of such groups are part of the ring and the oxygen and sulfur atoms are substituents on the ring;

15 R<sup>1</sup> is C<sub>1</sub>-C<sub>6</sub> alkyl optionally substituted with from one or two substituents independently selected from hydroxy, fluoro, chloro, bromo, iodo, C<sub>1</sub>-C<sub>4</sub> alkoxy, CF<sub>3</sub>, -C(=O)(C<sub>1</sub>-C<sub>4</sub> alkyl), -C(=O)-O-(C<sub>1</sub>-C<sub>4</sub>)alkyl, -OC(=O)(C<sub>1</sub>-C<sub>4</sub> alkyl), -OC(=O)N(C<sub>1</sub>-C<sub>4</sub> alkyl), -NHCO(C<sub>1</sub>-C<sub>4</sub> alkyl), -COOH, -COO(C<sub>1</sub>-C<sub>4</sub> alkyl), -CONH(C<sub>1</sub>-C<sub>4</sub> alkyl), -CON(C<sub>1</sub>-C<sub>4</sub> alkyl)(C<sub>1</sub>-C<sub>2</sub> alkyl), -S(C<sub>1</sub>-C<sub>4</sub> alkyl), -CN, -NO<sub>2</sub>, -SO(C<sub>1</sub>-C<sub>4</sub> alkyl), -SO<sub>2</sub>(C<sub>1</sub>-C<sub>4</sub> alkyl), -SO<sub>2</sub>NH(C<sub>1</sub>-C<sub>4</sub> alkyl) and -SO<sub>2</sub>N(C<sub>1</sub>-C<sub>4</sub> alkyl)(C<sub>1</sub>-C<sub>2</sub> alkyl), wherein each of the C<sub>1</sub>-C<sub>4</sub> alkyl groups in the foregoing R<sup>1</sup> groups may optionally contain one or two double or triple bonds;

20 R<sup>2</sup> is C<sub>1</sub>-C<sub>12</sub> alkyl which may optionally contain from one to three double or triple bonds, aryl or (C<sub>1</sub>-C<sub>4</sub> alkylene)aryl, wherein said aryl and the aryl moiety of said (C<sub>1</sub>-C<sub>4</sub> alkylene)aryl is selected from phenyl, naphthyl, thienyl, benzothienyl, pyridyl, quinolyl, pyrazinyl, pyrimidinyl, imidazolyl, furanyl, benzofuranyl, benzothiazolyl, 25 isothiazolyl, pyrazolyl, pyrrolyl, indolyl, pyrrolopyridyl, oxazolyl and benzoxazolyl; C<sub>3</sub>-C<sub>8</sub> cycloalkyl or (C<sub>1</sub>-C<sub>6</sub> alkylene)(C<sub>3</sub>-C<sub>8</sub> cycloalkyl), wherein one or two of the carbon atoms of said cycloalkyl and the 5 to 8 membered cycloalkyl moieties of said (C<sub>1</sub>-C<sub>6</sub> alkylene)(C<sub>3</sub>-C<sub>8</sub> cycloalkyl) may optionally and independently be replaced by an oxygen or sulfur atom or by NZ wherein Z is hydrogen, C<sub>1</sub>-C<sub>4</sub> alkyl or benzyl, and 30 wherein each of the foregoing R<sup>2</sup> groups may optionally be substituted with from one to three substituents independently selected from chloro, fluoro, hydroxy and C<sub>1</sub>-C<sub>4</sub> alkyl, or with one substituent selected from C<sub>1</sub>-C<sub>6</sub> alkoxy, -OC(=O)(C<sub>1</sub>-C<sub>6</sub> alkyl), -OC(=O)N(C<sub>1</sub>-C<sub>4</sub> alkyl)(C<sub>1</sub>-C<sub>2</sub> alkyl), -S(C<sub>1</sub>-C<sub>6</sub> alkyl), amino, -NH(C<sub>1</sub>-C<sub>2</sub> alkyl), -N(C<sub>1</sub>-C<sub>2</sub> alkyl)(C<sub>1</sub>-C<sub>4</sub> alkyl), -N(C<sub>1</sub>-C<sub>4</sub> alkyl)-CO-(C<sub>1</sub>-C<sub>4</sub> alkyl), -NHCO(C<sub>1</sub>-C<sub>4</sub> alkyl), -COOH,

-COO(C<sub>1</sub>-C<sub>4</sub> alkyl), -CONH(C<sub>1</sub>-C<sub>4</sub> alkyl), -CON(C<sub>1</sub>-C<sub>4</sub> alkyl)(C<sub>1</sub>-C<sub>2</sub> alkyl), -SH, -CN, -NO<sub>2</sub>, -SO(C<sub>1</sub>-C<sub>4</sub> alkyl), -SO<sub>2</sub>(C<sub>1</sub>-C<sub>4</sub> alkyl), -SO<sub>2</sub>NH(C<sub>1</sub>-C<sub>4</sub> alkyl) and -SO<sub>2</sub>N(C<sub>1</sub>-C<sub>4</sub> alkyl)(C<sub>1</sub>-C<sub>2</sub> alkyl);

-NR<sup>1</sup>R<sup>2</sup> or CR<sup>1</sup>R<sup>2</sup>R<sup>10</sup> may form a ring selected from saturated 3 to 8

5 membered rings, the 5 to 8 membered rings of which may optionally contain one or two double bonds, and wherein one or two of the ring carbon atoms of such 5 to 8 membered rings may optionally and independently be replaced by an oxygen or sulfur atom or by NZ<sup>2</sup> wherein Z<sup>2</sup> is hydrogen, benzyl or C<sub>1</sub>-C<sub>4</sub> alkyl;

R<sup>3</sup> is hydrogen, C<sub>1</sub>-C<sub>4</sub> alkyl, -O(C<sub>1</sub>-C<sub>4</sub> alkyl), chloro, fluoro, bromo, iodo,

10 -S(C<sub>1</sub>-C<sub>4</sub> alkyl) or -SO<sub>2</sub>(C<sub>1</sub>-C<sub>4</sub> alkyl);

each R<sup>8</sup>, R<sup>9</sup> and R<sup>12</sup> is selected, independently, from hydrogen and C<sub>1</sub>-C<sub>2</sub> alkyl;

each R<sup>4</sup> and R<sup>6</sup> that is attached to a carbon atom is selected, independently, from hydrogen and C<sub>1</sub>-C<sub>6</sub> alkyl, fluoro, chloro, bromo, iodo, hydroxy, hydroxy (C<sub>1</sub>-C<sub>2</sub>

15 alkyl), trifluoromethyl, cyano, amino, nitro, -O(C<sub>1</sub>-C<sub>4</sub> alkyl), -N(C<sub>1</sub>-C<sub>4</sub> alkyl)(C<sub>1</sub>-C<sub>2</sub> alkyl), -CH<sub>2</sub>SCH<sub>3</sub>, -S(C<sub>1</sub>-C<sub>4</sub> alkyl), -CO(C<sub>1</sub>-C<sub>4</sub> alkyl), -C(=O)H or -C(=O)O(C<sub>1</sub>-C<sub>4</sub> alkyl), wherein each of the C<sub>1</sub>-C<sub>2</sub> alkyl moieties in the foregoing R<sup>4</sup> and R<sup>6</sup> groups may optionally contain one double or triple bond; and R<sup>6</sup>, when attached to a nitrogen atom, is selected from hydrogen and C<sub>1</sub>-C<sub>4</sub> alkyl;

20 R<sup>5</sup> is substituted phenyl, naphthyl, pyridyl or pyrimidyl, wherein each of the foregoing R<sup>5</sup> groups is substituted with from two to four substituents R<sup>13</sup>, wherein up to three of said substituents may be selected, independently, from chloro, C<sub>1</sub>-C<sub>6</sub> alkyl, -O(C<sub>1</sub>-C<sub>6</sub> alkyl) and -(C<sub>1</sub>-C<sub>6</sub> alkylene)O(C<sub>1</sub>-C<sub>6</sub> alkyl), and wherein one of said substituents may be selected, independently, from bromo, iodo, formyl, cyano,

25 trifluoromethyl, nitro, amino, -NH(C<sub>1</sub>-C<sub>4</sub> alkyl), -N(C<sub>1</sub>-C<sub>2</sub> alkyl)(C<sub>1</sub>-C<sub>6</sub> alkyl), -C(=O)O(C<sub>1</sub>-C<sub>4</sub> alkyl), -C(=O)(C<sub>1</sub>-C<sub>4</sub> alkyl), -COOH, -SO<sub>2</sub>NH(C<sub>1</sub>-C<sub>4</sub> alkyl), -SO<sub>2</sub>N(C<sub>1</sub>-C<sub>2</sub> alkyl)(C<sub>1</sub>-C<sub>4</sub> alkyl), -SO<sub>2</sub>NH<sub>2</sub>, -NHSO<sub>2</sub>(C<sub>1</sub>-C<sub>4</sub> alkyl), -(C<sub>0</sub>-C<sub>1</sub>alkylene)-S-(C<sub>1</sub>-C<sub>2</sub>alkyl), -(C<sub>0</sub>-C<sub>1</sub>alkylene)-SO-(C<sub>1</sub>-C<sub>2</sub>alkyl), -(C<sub>0</sub>-C<sub>1</sub>alkylene)-SO<sub>2</sub>-(C<sub>1</sub>-C<sub>2</sub>alkyl) and -(C<sub>1</sub>-C<sub>4</sub>alkylene)-OH, and wherein each of the C<sub>1</sub>-C<sub>4</sub> alkyl and C<sub>1</sub>-C<sub>6</sub> alkyl moieties in

30 the foregoing R<sup>5</sup> groups may optionally be substituted with one or two substituents independently selected from fluoro, hydroxy, amino, methylamino, dimethylamino and acetyl;

R<sup>7</sup> is hydrogen, methyl, halo (e.g., chloro, fluoro, iodo or bromo), hydroxy, methoxy, -C(=O)(C<sub>1</sub>-C<sub>2</sub> alkyl), -C(=O)O(C<sub>1</sub>-C<sub>2</sub> alkyl), hydroxymethyl, trifluoromethyl or formyl;

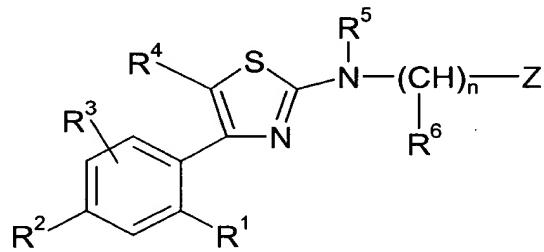
R<sup>10</sup> is hydrogen, hydroxy, methoxy or fluoro; and

5 R<sup>11</sup> is hydrogen or C<sub>1</sub>-C<sub>4</sub> alkyl;

with the proviso that in the ring containing D, E, K and G of formula I, there can not be two double bonds adjacent to each other;

and the pharmaceutically acceptable salt of such compound.

10 10. A pharmaceutical composition according to claim 1 wherein said corticotropin releasing factor antagonist is a compound of formula

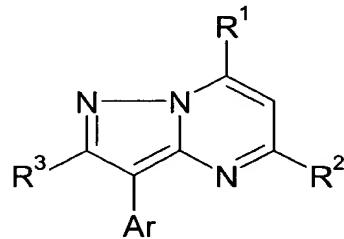


wherein each of R<sup>1</sup> and R<sup>2</sup> is independently a halogen atom; a C<sub>1</sub>-C<sub>5</sub> hydroxyalkyl radical; C<sub>1</sub>-C<sub>5</sub> alkyl; C<sub>7</sub>-C<sub>10</sub> aralkyl; C<sub>1</sub>-C<sub>5</sub> alkoxy; trifluoromethyl; nitro; nitrile; a group -

15 SR where R is hydrogen, a C<sub>1</sub>-C<sub>5</sub> alkyl radical or a C<sub>7</sub>-C<sub>10</sub> aralkyl radical; a group S-CO-R where R is a C<sub>1</sub>-C<sub>5</sub> alkyl radical or aralkyl in which the aryl portion is C<sub>6</sub>-C<sub>8</sub> and the alkyl portion is C<sub>1</sub>-C<sub>4</sub>; a group -COOR' where R' is hydrogen or C<sub>1</sub>-C<sub>5</sub> alkyl; a group -CONR'R" where R' and R" are as defined above for R'; a group -NR'R" where R' and R" are as previously defined for R'; a group -CONRaRb or NRaRb, where Ra 20 and Rb, taken together with the nitrogen atom to which they are attached, form a 5- to 7-membered heterocyclic ring; or a group -NHCO-NR'R", where R' and R" are as defined above for R'; R<sup>3</sup> is hydrogen or as defined for R<sup>1</sup> and R<sup>2</sup> is a hydrogen atom; C<sub>1</sub>-<sub>5</sub> alkyl; halogen; a hydroxymethyl group; or a formyl group; R<sup>5</sup> is C<sub>1</sub>-C<sub>5</sub> alkyl; a C<sub>3</sub>-C<sub>7</sub> cycloalkyl group; a cycloalkylalkyl group in which the cycloalkyl portion is C<sub>3</sub>-C<sub>7</sub> 25 and the alkyl portion is C<sub>1</sub>-C<sub>5</sub>; or C<sub>5</sub>-C<sub>6</sub> alkenyl; n is 0 or 1; R<sup>6</sup> is C<sub>1</sub>-<sub>5</sub> alkyl; alkoxyalkyl in which the alkyl portions are C<sub>1</sub>-C<sub>5</sub>; C<sub>3</sub>-C<sub>7</sub> cycloalkyl; a cycloalkylalkyl group in which the cycloalkyl portion is C<sub>3</sub>-C<sub>7</sub> and the alkyl portion is C<sub>1</sub>-C<sub>5</sub>; a cycloalkyloxyalkyl radical in which the cycloalkyl is C<sub>3</sub>-C<sub>7</sub> and the alkyl is C<sub>1</sub>-C<sub>4</sub>; a hydroxyalkyloxyalkyl radical in which the alkyls are C<sub>2</sub>-C<sub>10</sub>; or an alkoxyalkyloxyalkyl radical in which the

alkyls are C<sub>3</sub>-C<sub>12</sub>; and Z is an optionally substituted bi- or tricyclic aromatic or heteroaromatic group; and stereoisomers and/or addition salts thereof.

11. A pharmaceutical composition according to claim 1 wherein said  
5 corticotropin releasing factor antagonist is a compound of formula



including the stereoisomers and the pharmaceutically acceptable acid addition salt forms thereof, wherein

R<sup>1</sup> is NR<sup>4</sup>R<sup>5</sup> or OR<sup>5</sup>;

10 R<sup>2</sup> is C<sub>1</sub>-C<sub>6</sub>alkyl, C<sub>1</sub>-C<sub>6</sub>alkyloxy or C<sub>1</sub>-C<sub>6</sub>alkylthio;

R<sup>3</sup> is hydrogen, C<sub>1</sub>-C<sub>6</sub>alkyl, C<sub>1</sub>-C<sub>6</sub>alkylsulfonyl, C<sub>1</sub>-C<sub>6</sub>alkylsulfoxy or C<sub>1</sub>-C<sub>6</sub>alkylthio;

R<sup>4</sup> is hydrogen, C<sub>1</sub>-C<sub>6</sub>alkyl, mono- or di(C<sub>3</sub>-C<sub>6</sub>cycloalkylmethyl, C<sub>3</sub>-C<sub>6</sub>cycloalkyl, C<sub>3</sub>-C<sub>6</sub>alkenyl, hydroxyC<sub>1</sub>-C<sub>6</sub>alkyl, C<sub>1</sub>-C<sub>6</sub>alkylcarbonyloxyC<sub>1</sub>-C<sub>6</sub>alkyl or C<sub>1</sub>-C<sub>6</sub>alkyloxyC<sub>1</sub>-C<sub>6</sub>alkyl;

15 R<sup>5</sup> is C<sub>1</sub>-C<sub>8</sub>alkyl, mono- or di(C<sub>3</sub>-C<sub>6</sub>cycloalkyl)methyl, Ar<sup>1</sup>CH<sub>2</sub>, C<sub>3</sub>-C<sub>6</sub>alkenyl, C<sub>1</sub>-C<sub>6</sub>alkyloxyC<sub>1</sub>-C<sub>6</sub>alkyl, hydroxyC<sub>1</sub>-C<sub>6</sub>alkyl, thiethylmethyl, furethylmethyl, C<sub>1</sub>-C<sub>6</sub>alkylthioC<sub>1</sub>-C<sub>6</sub>alkyl, morpholinyl, mono- or di(C<sub>1</sub>-C<sub>6</sub>alkyl)aminoC<sub>1</sub>-C<sub>6</sub>alkyl, di(C<sub>1</sub>-C<sub>6</sub>alkyl)amino, C<sub>1</sub>-C<sub>6</sub>alkylcarbonylC<sub>1</sub>-C<sub>6</sub>alkyl, C<sub>1</sub>-C<sub>6</sub>alkyl substituted with imidazolyl; or

20 a radical of formula -Alk-O-CO-Ar<sup>1</sup>;

or R<sup>4</sup> and R<sup>5</sup> taken together with the nitrogen atom to which they are attached may form a pyrrolidinyl, piperidinyl, homopiperidinyl or morpholinyl group, optionally substituted with C<sub>1</sub>-C<sub>6</sub>alkyl or C<sub>1</sub>-C<sub>6</sub>alkyloxyC<sub>1</sub>-C<sub>6</sub>alkyl; and

Ar is phenyl; phenyl substituted with 1, 2 or 3 substituents independently selected from halo, C<sub>1</sub>-C<sub>6</sub>alkyl, trifluoromethyl, hydroxy, cyano, C<sub>1</sub>-C<sub>6</sub>alkyloxy, benzyloxy, C<sub>1</sub>-C<sub>6</sub>alkylthio, nitro, amino and mono- or di(C<sub>1</sub>-C<sub>6</sub>alkyl)amino; pyridinyl; pyridinyl substituted with 1 ~ 2 or 3 substituents independently selected from halo, C<sub>1</sub>-C<sub>6</sub>alkyl, trifluoromethyl, hydroxy, cyano, C<sub>1</sub>-C<sub>6</sub>alkyloxy, benzyloxy, C<sub>1</sub>-C<sub>6</sub>alkylthio,

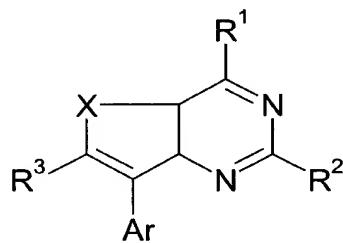
nitro, amino, mono- or di(C<sub>1</sub>-C<sub>6</sub>alkyl)amino and piperidinyl; and wherein said substituted phenyl may optionally be further substituted with one or more halogens;

Ar<sup>1</sup> is phenyl; phenyl substituted with 1, 2 or 3 substituents each independently selected from halo, C<sub>1</sub>-C<sub>6</sub>alkyl, C<sub>1</sub>-C<sub>6</sub>alkyloxy, di(C<sub>1</sub>-C<sub>6</sub>alkyl)aminoC<sub>1</sub>-C<sub>6</sub>alkyl, trifluoromethyl and C<sub>1</sub>-C<sub>6</sub>alkyl substituted with morpholinyl; or pyridinyl; and Alk is C<sub>1</sub>-C<sub>6</sub>alkanediyl;

5 with the proviso that 5-methyl-3-phenyl-7-(phenylmethoxy)-pyrazolo[1,5-a]pyrimidine and 2,5-dimethyl-7-(methylamino)-3-phenyl-pyrazolo[1,5-a]pyrimidine are not included.

10

12. A pharmaceutical composition according to claim 1 wherein said corticotropin releasing factor antagonist is a compound of formula



15 including the stereoisomers and the pharmaceutically acceptable acid addition salt forms thereof, wherein

X is S, SO or S0<sub>2</sub>;

R<sup>1</sup> is NR<sup>4</sup>R<sup>5</sup> or OR<sup>5</sup>;

R<sup>2</sup> is C<sub>1</sub>-C<sub>6</sub>alkyl, C<sub>1</sub>-C<sub>6</sub>alkyloxy or C<sub>1</sub>-C<sub>6</sub>alkylthio;

20 R<sup>3</sup> is hydrogen, C<sub>1</sub>-C<sub>6</sub>alkyl, C<sub>1</sub>-C<sub>6</sub>alkylsulfonyl, C<sub>1</sub>-C<sub>6</sub>alkylsulfoxy or C<sub>1</sub>-C<sub>6</sub>alkylthio;

R<sup>4</sup> is hydrogen, C<sub>1</sub>-alkyl, mono- or di(C<sub>3</sub>-C<sub>6</sub>cycloalkyl)methyl, C<sub>3</sub>-C<sub>6</sub>cycloalkyl, C<sub>3</sub>-C<sub>6</sub>alkenyl, hydroxyC<sub>1</sub>-C<sub>6</sub>alkyl, C<sub>1</sub>-C<sub>6</sub>alkylcarbonyloxyC<sub>1</sub>-C<sub>6</sub>alkyl or C<sub>1</sub>-C<sub>6</sub>alkyloxyC<sub>1</sub>-C<sub>6</sub>alkyl;

25 R<sup>5</sup> is C<sub>1</sub>-C<sub>6</sub>alkyl, mono- or di(C<sub>3</sub>-C<sub>6</sub>cycloalkyl)methyl, Ar<sup>1</sup>CH<sub>2</sub>, C<sub>3</sub>-C<sub>6</sub>alkenyl, C<sub>1</sub>-C<sub>6</sub>alkyloxyC<sub>1</sub>-C<sub>6</sub>alkyl, hydroxyC<sub>1</sub>-C<sub>6</sub>alkyl, thienylmethyl, furanylmethyl, C<sub>1</sub>-C<sub>6</sub>alkylthioC<sub>1</sub>-C<sub>6</sub>alkyl, morpholinyl, mono- or di(C<sub>1</sub>-C<sub>6</sub>alkyl)aminoC<sub>1</sub>-C<sub>6</sub>alkyl, di(C<sub>1</sub>-C<sub>6</sub>alkyl)amino, C<sub>1</sub>-C<sub>6</sub>alkylcarbonylC<sub>1</sub>-C<sub>6</sub>alkyl, C<sub>1</sub>-C<sub>6</sub>alkyl substituted with imidazolyl; or a radical of formula -Alk-O-CO-Ar I;

or R<sup>4</sup> and R<sup>5</sup> taken together with the nitrogen atom to which they are attached may form a pyrrolidinyl, piperidinyl, homopiperidinyl or morpholinyl group, optionally substituted with C<sub>1</sub>-C<sub>6</sub>alkyl or C<sub>1</sub>-C<sub>6</sub>alkyloxyC<sub>1</sub>-C<sub>6</sub>alkyl;

Ar is phenyl; phenyl substituted with 1, 2 or 3 substituents independently selected from halo, C<sub>1</sub>-C<sub>6</sub>alkyl, trifluoromethyl, hydroxy, cyano, C<sub>1</sub>-C<sub>6</sub>alkyloxy, benzyloxy, C<sub>1</sub>-C<sub>6</sub>alkylthio, nitro, amino and mono- or di(C<sub>1</sub>-C<sub>6</sub>alkyl)amino; pyridinyl; pyridinyl substituted with 1, 2 or 3 substituents independently selected from halo, C<sub>1</sub>-C<sub>6</sub>alkyl, trifluoromethyl, hydroxy, cyano, C<sub>1</sub>-C<sub>6</sub>alkyloxy, benzyloxy, C<sub>1</sub>-C<sub>6</sub>alkylthio, nitro, amino, mono- or di(C<sub>1</sub>-C<sub>6</sub>alkyl)amino and piperidinyl; and wherein said substituted phenyl may optionally be further substituted with one or more halogens;

Ar<sup>1</sup> is phenyl; phenyl substituted with 1, 2 or 3 substituents each independently selected from halo, C<sub>1</sub>-C<sub>6</sub>alkyl, C<sub>1</sub>-C<sub>6</sub>alkyloxy, di(C<sub>1</sub>-C<sub>6</sub>alkyl)aminoC<sub>1</sub>-C<sub>6</sub>alkyl trifluoromethyl, and C<sub>1</sub>-C<sub>6</sub>alkyl substituted with morpholinyl; or pyridinyl; and Alk is C<sub>1</sub>-C<sub>6</sub>alkanediyl.

13. A pharmaceutical composition according to claim 1 wherein said corticotropin releasing factor antagonist is a compound selected from the group consisting of:

4-(1-ethyl-propoxy)-3,6-dimethyl-2-(2,4,6-trimethylphenoxy)-pyridine;

butyl-[2,5-dimethyl-7-(2,4,6-trimethylphenyl)-6,7-dihydro-5H-pyrrolo[2,3-d]pyrimidin-4-yl]-ethyl-amine;

4-(butyl-ethylamino)-2,5-dimethyl-7-(2,4,6-trimethylphenyl)-5,7-dihydro-pyrrolo[2,3-d]pyrimidin-6-one;

4-(1-ethylpropoxy)-2,5-dimethyl-6-(2,4,6-trimethylphenoxy)-pyrimidine;

N-butyl-N-ethyl-2,5-dimethyl-NN-(2,4,6-trimethylphenyl)-pyrimidine-4,6-diamine;

[4-(1-ethyl-propoxy)-3,6-dimethyl-pyridin-2-yl]-(2,4,6-trimethylphenyl)-amine;

6-(ethyl-propyl-amino)-2,7-dimethyl-9-(2,4,6-trimethylphenyl)-7,9-dihydro-purin-8-one;

3-{(4-methyl-benzyl)-[3,6-dimethyl-1-(2,4,6-trimethylphenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yl]-amino}-propan-1-ol;

diethyl-[6-methyl-3-methylsulfanyl-1-(2,4,6-trichlorophenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yl]-amine;

2-(butyl-[6-methyl-3-methylsulfanyl-1-(2,4,6-trichlorophenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yl]-amino)-ethanol;

5 dibutyl-[6-methyl-3-methylsulfanyl-1-(2,4,6-trichlorophenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yl]-amine;

10 butyl-ethyl-[6-methyl-3-methylsulfanyl-1-(2,4,6-trichlorophenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yl]-amine;

15 butyl-ethyl-[6-methyl-3-methylsulfonyl-1-(2,4,6-trichlorophenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yl]-amine;

20 butyl-cyclopropylmethyl-[6-methyl-3-methylsulfanyl-1-(2,4,6-trichlorophenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yl]-amine;

25 di-1-propyl-[6-methyl-3-methylsulfanyl-1-(2,4,6-trichlorophenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yl]-amine;

30 butyl-ethyl-[6-chloro-3-methylsulfanyl-1-(2,4,6-trichlorophenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yl]-amine;

35 butyl-ethyl-[6-methoxy-3-methylsulfanyl-1-(2,4,6-trichlorophenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yl]-amine;

40 propyl-ethyl-[3,6-dimethyl-1-(2,4,6-trimethylphenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yl]-amine;

45 4-(1-ethyl-propyl)-6-methyl-3-methylsulfanyl-1-(2,4,6-trimethylphenyl)-1H-pyrazolo[3,4-d]pyrimidine;

50 n-butyl-ethyl-[2,5-dimethyl-7-(2,4,6-trimethylphenyl)-7H-pyrrolo[2,3-d]pyrimidin-4-yl]amine;

55 di-n-propyl-[2,5-dimethyl-7-(2,4,6-trimethylphenyl)-7H-pyrrolo[2,3-d]pyrimidin-4-yl]amine;

60 diethyl-2,5-dimethyl-7-(2,4,6-trimethylphenyl)-7H-pyrrolo[2,3-d]pyrimidin-4-yl]amine;

65 n-butyl-ethyl-[2,5,6-trimethyl-7-(2,4,6-trimethylphenyl)-7H-pyrrolo[2,3-d]pyrimidin-4-yl]amine;

70 2-{N-n-butyl-N-[2,5-dimethyl-7-(2,4,6-trimethylphenyl)-7H-pyrrolo[2,3-d]pyrimidin-4-yl]amino}-ethanol;

4-(1-ethyl-propyl)-2,5,6-trimethyl-7-(2,4,6-trimethylphenyl)-7H-pyrrolo[2,3-d]pyrimidine;

n-butyl-ethyl-[2,5-dimethyl-7-(2,4-dimethylphenyl)-7H-pyrrolo[2,3-d]pyrimidin-4-yl]amine;

5 2,5-dimethyl-7-(2,4,6-trimethylphenyl)-7H-pyrrolo[2,3-d]pyrimidyl-4-yl)-(1-ethyl-propyl)amine;

butyl-[3,6-dimethyl-1-(2,4,6-trimethylphenyl)-1H-pyrazolo[3,4-b]pyridin-4-yl]-ethylamine;

[3,6-dimethyl-1-(2,4,6-trimethylphenyl)-1H-pyrazolo[3,4,b]pyridin-4-yl]-(1-methoxymethylpropyl)-amine;

10 4-(1-methoxymethylpropoxy)-3,6-dimethyl-1-(2,4,6-trimethylphenyl)-1H-pyrazolo[3,4-b]pyridine;

(1-ethylpropyl)-[3,5,6-trimethyl-1-(2,4,6-trimethylphenyl)-1H-pyrazolo[3,4-b]pyridin-4-yl]-amine;

15 4-(1-ethylpropoxy)-2,5-dimethyl-7-(2,4,6-trimethylphenyl)-7H-pyrrolo[2,3-b]pyridine;

4-(1-ethylpropoxy)-2,5,6-trimethyl-7-(2,4,6-trimethylphenyl)-7H-pyrrolo[2,3-b]pyridine;

4-(1-ethylpropoxy)-2,5-dimethyl-7-(2,6-dimethyl-4-bromophenyl)-7H-pyrrolo[2,3-b]pyridine;

20 2,5,6-trimethyl-7-(1-propylbutyl)-4-(2,4,6-trimethylphenoxy)-7H-pyrrolo[2,3-d]pyrimidine;

1-(1-ethylpropyl)-6-methyl-4-(2,4,6-trimethylphenylamino)-1,3-dihydro-imidazo[4,5-c]pyridin-2-one;

25 9-(1-ethylpropyl)-2-methyl-6-(2,4,6-trimethylphenylamino)-7,9-dihydro-purin-8-one;

1-(1-ethylpropyl)-6-methyl-4-(2,4,6-trimethylphenoxy)-1,3-dihydro-imidazo[4,5-c]pyridin-2-one;

30 1-(1-ethylpropyl)-6-methyl-4-(2,4,6-trimethylphenoxy)-1H-imidazo[4,5-c]pyridine;

1-(1-ethylpropyl)-3,6-dimethyl-4-(2,4,6-trimethylphenoxy)-1,3-dihydro-imidazo[4,5-c]pyridin-2-one;

1-(1-ethylpropyl)-3,6-dimethyl-4-(2,4,6-trimethylphenylamino)-1,3-dihydro-imidazo[4,5-c]pyridin-2-one;

1-(1-ethyl-propyl)-4,7-dimethyl-5-(2,4,6-trimethyl-phenoxy)-1,4-dihydro-2H-pyrido[3,4-b]pyrazin-3-one;

1-(1-ethyl-propyl)-4,7-dimethyl-5-(2,4,6-trimethyl-phenoxy)-1,2,3,4-tetrahydro-pyrido[3,4-b]pyrazine;

5 1-(1-ethyl-propyl)-7-methyl-5-(2,4,6-trimethyl-phenoxy)-1,2,3,4-tetrahydro-pyrido[3,4-b]pyrazine;

1-(1-ethyl-propyl)-7-methyl-2-oxo-5-(2,4,6-trimethyl-phenoxy)-1,2,3,4-tetrahydro-[1,6]naphthyridine-3-carboxylic acid methyl ester;

10 1-(1-ethyl-propyl)-7-methyl-2-oxo-5-(2,4,6-trimethyl-phenoxy)-1,2,3,4-tetrahydro-[1,6]naphthyridine-3-carboxylic acid isopropyl ester;

1-(1-ethyl-propyl)-7-methyl-5-(2,4,6-trimethyl-phenoxy)-3,4-dihydro-1H-[1,6]naphthyridin-2-one;

15 1-(1-ethyl-propyl)-7-methyl-5-(2,4,6-trimethyl-phenoxy)-1,2,3,4-tetrahydro-[1,6]naphthyridine;

1-(1-ethyl-propyl)-7-methyl-5-(2,4,6-trimethyl-phenoxy)-1,4-dihydro-2H-3-oxa-1,6-diaza-naphthalene;

20 1-(1-ethyl-propyl)-4,7-dimethyl-5-(2,4,6-trimethyl-phenoxy)-1,4-dihydro-2H-3-oxa-1,6-diaza-naphthalene;

1-(1-ethyl-propyl)-3,7-dimethyl-5-(2,4,6-trimethyl-phenoxy)-3,4-dihydro-1H-3-oxa-[1,6]-naphthyridin-2-one;

25 1-(1-ethyl-propyl)-3,3,6-trimethyl-4-(2,4,6-trimethyl-phenoxy)-2,3-dihydro-1H-pyrrolo[3,2-c]pyridine;

7-(1-ethyl-propoxy)-5-methyl-3-(2,4,6-trimethyl-phenyl)-pyrazolo[1,5-a]pyrimidine;

30 [2,5-dimethyl-3-(2,4,6-trimethyl-phenyl)-pyrazolo[1,5-a]pyrimidin-7-yl]-(1-ethyl-propyl)-amine;

(1-ethyl-propyl)-[5-methyl-3-(2,4,6-trimethyl-phenyl)-pyrazolo[1,5-a]pyrimidin-7-yl]-amine;

7-(1-ethyl-propoxy)-2,5-dimethyl-3-(2,4,6-trimethyl-phenyl)-pyrazolo[1,5-a]pyrimidine;

[2,5-dimethyl-3-(2,4,6-trimethyl-phenyl)-pyrazolo[1,5-a]pyrimidin-7-yl]-ethyl-propyl-amine;

[6-bromo-5-bromomethyl-3-(2,4,6-trimethyl-phenyl)-3H-[1,2,3]triazolo[4,5-b]pyridin-7-yl]-(1-ethyl-propyl)-amine;

(1-ethyl-propyl)-[5-methyl-3-(2,4,6-trimethyl-phenyl)-3H-[1,2,3]triazolo[4,5-b]pyridin-7-yl]-amine;

[6-bromo-5-methyl-3-(2,4,6-trimethyl-phenyl)-3H-[1,2,3]triazolo[4,5-b]pyridin-7-yl]- (1-ethyl-propyl)-methyl-amine;

5 7-(1-ethyl-propoxy)-5-methyl-3-(2,4,6-trimethyl-phenyl)-3H-[1,2,3]triazolo[4,5-b]pyridine;

4-(1-ethyl-propoxy)-2,5-dimethyl-7-(2,4,6-trimethyl-phenyl)-5H-pyrrolo[3,2-d]pyrimidine;

( $\pm$ )-2,5-dimethyl-4-(tetrahydro-furan-3-yloxy)-7-(2,4,6-trimethyl-phenyl)-5H-pyrrolo-[3,2-d]pyrimidine;

10 2,5-dimethyl-4-(S)-(tetrahydro-furan-3-yloxy)-7-(2,4,6-trimethyl-phenyl)-5H-pyrrolo-[3,2-d]pyrimidine;

2,5-dimethyl-4-(1-propyl-butoxy)-7-(2,4,6-trimethyl-phenyl)-5H-pyrrolo[3,2-d]pyrimidine;

15 4-sec-butylsulfanyl-2,5-dimethyl-7-(2,4,6-trimethyl-phenyl)-5H-pyrrolo[3,2-d]pyrimidine;

4-(butyl-ethyl-amino)-2,6-dimethyl-8-(2,4,6-trimethyl-phenyl)-5,8-dihydro-6H-pyrido[2,3-d]pyrimidin-7-one;

8-(1-ethyl-propoxy)-6-methyl-4-(2,4,6-trimethyl-phenyl)-3,4-dihydro-1H-pyrido[2,3-b] pyrazin-2-one;

20 8-(1-ethyl-propoxy)-6-methyl-4-(2,4,6-trimethyl-phenyl)-1,2,3,4-tetrahydro-pyrido [2,3-b]pyrazine;

4-(1-ethyl-propoxy)-2-methyl-8-(2,4,6-trimethyl-phenyl)-quinoline;

25 5-(1-ethyl-propoxy)-7-methyl-1-(2,4,6-trimethyl-phenyl)-1,4-dihydro-2H-3-oxa-1,8-diaza-naphthalene;

5-(1-ethyl-propoxy)-7-methyl-1-(2,4,6-trimethyl-phenyl)-1,2-dihydro-3-oxa-1,8-diaza-naphthalen-4-one;

8-(1-ethyl-propoxy)-1,6-dimethyl-4-(2,4,6-trimethyl-phenyl)-1,2,3,4-tetrahydro-pyrido[2,3-b]pyrazine;

30 (1-ethyl-propyl)-[2-methyl-8-(2,4,6-trimethyl-phenyl)-quinolin-4-yl]-amine;

4-(butyl-ethyl-amino)-2,6-dimethyl-8-(2,6-dimethyl-4-bromo-phenyl)-5,8-dihydro-6H-pyrido[2,3-d]pyrimidin-7-one;

4-(butyl-ethyl-amino)-2-methyl-8-(2,6-dimethyl-4-bromo-phenyl)-5,8-dihydro-6H- pyrido[2,3-d]pyrimidin-7-one;

4-(1-ethyl-propoxy)-2-methyl-8-(2,6-dimethyl-4-bromo-phenyl)-5,8-dihydro-6H-pyrido[2,3-d]pyrimidin-7-one;  
· (butyl-ethyl)-[2-methyl-8-(2,6-dimethyl-4-bromo-phenyl)-5,6,7,8-tetrahydro-pyrido[2,3-d]pyrimidin-4-yl]-amine;  
5 (propyl-ethyl)-[2-methyl-8-(2,6-dimethyl-4-bromo-phenyl)-5,6,7,8-tetrahydro-pyrido[2,3-d]pyrimidin-4-yl]-amine;  
· (diethyl)-[2-methyl-8-(2,6-dimethyl-4-bromo-phenyl)-5,6,7,8-tetrahydro-pyrido[2,3-d]pyrimidin-4-yl]-amine;  
· (1-ethyl-propyl)-[2-methyl-8-(2,6-dimethyl-4-bromo-phenyl)-5,6,7,8-tetrahydro-pyrido[2,3-d]pyrimidin-4-yl]-amine;  
10 (1-ethyl-propoxy)-2-methyl-8-(2,6-dimethyl-4-bromo-phenyl)-5,6,7,8-tetrahydro-pyrido[2,3-d]pyrimidin-7-one;  
· 4-(butyl-ethyl-amino)-2-methyl-8-(2,4,6-trimethyl-phenyl)-5,8-dihydro-6H-pyrido[2,3-d]pyrimidin-7-one;  
15 4-(1-ethyl-propoxy)-2-methyl-8-(2,4,6-trimethyl-phenyl)-5,8-dihydro-6H-pyrido[2,3-d]pyrimidin-7-one;  
· (butyl-ethyl)-[2-methyl-8-(2,4,6-trimethyl-phenyl)-5,6,7,8-tetrahydro-pyrido[2,3-d]pyrimidin-4-yl]-amine;  
· (propyl-ethyl)-[2-methyl-8-(2,4,6-trimethyl-phenyl)-5,6,7,8-tetrahydro-pyrido[2,3-d]pyrimidin-4-yl]-amine;  
20 (1-ethyl-propyl)-[2-methyl-8-(2,4,6-trimethyl-phenyl)-5,6,7,8-tetrahydro-pyrido[2,3-d]pyrimidin-4-yl]-amine;  
· (diethyl)-[2-methyl-8-(2,4,6-trimethyl-phenyl)-5,6,7,8-tetrahydro-pyrido[2,3-d]pyrimidin-4-yl]-amine;  
· (1-ethyl-propyl)-[2-methyl-8-(2,4,6-trimethyl-phenyl)-5,6,7,8-tetrahydro-pyrido[2,3-d]pyrimidin-4-yl]-amine;  
25 (1-ethyl-propoxy)-2-methyl-8-(2,4,6-trimethyl-phenyl)-5,6,7,8-tetrahydro-pyrido[2,3-d]pyrimidin-7-one;  
· 8-(1-ethyl-propoxy)-6-methyl-4-(2,6-dimethyl-4-bromo-phenyl)-3,4-dihydro-1H-pyrido[2,3-b]pyrazin-2-one;  
· 8-(1-ethyl-propoxy)-6-methyl-4-(2,6-dimethyl-4-bromo-phenyl)-1,2,3,4-tetrahydro-pyrido[2,3-b]pyrazine;  
30 4-(1-ethyl-propoxy)-2-methyl-8-(2,6-dimethyl-4-bromo-phenyl)-quinoline;  
· 5-(1-ethyl-propoxy)-7-methyl-1-(2,6-dimethyl-4-bromo-phenyl)-1,4-dihydro-2H-3-oxa-1,8-diaza-naphthalene;

5-(1-ethyl-propoxy)-7-methyl-1-(2,6-dimethyl-4-bromo-phenyl)-1,2-dihydro-3-oxa-1,8-diaza-naphthalen-4-one;

8-(1-ethyl-propoxy)-1,6-dimethyl-4-(2,6-dimethyl-4-bromo-phenyl)-1,2,3,4-tetrahydro-pyrido[2,3-b]pyrazine;

5 (1-ethyl-propyl)-[2-methyl-8-(2,6-dimethyl-4-bromo-phenyl)-quinolin-4-yl]-amine;

4-(butyl-ethyl-amino)-2,6-dimethyl-8-(2,6-dimethyl-4-chloro-phenyl)-5,8-dihydro-6H-pyrido[2,3-d]pyrimidin-7-one;

8-(1-ethyl-propoxy)-6-methyl-4-(2,6-dimethyl-4-chloro-phenyl)-3,4-dihydro-1H-pyrido[2,3-b]pyrazin-2-one;

8-(1-ethyl-propoxy)-6-methyl-4-(2,6-dimethyl-4-chloro-phenyl)-1,2,3,4-tetrahydro- pyrido[2,3-b]pyrazine;

4-(1-ethyl-propoxy)-2-methyl-8-(2,6-dimethyl-4-chloro-phenyl)-quinoline;

5-(1-ethyl-propoxy)-7-methyl-1-(2,6-dimethyl-4-chloro-phenyl)-1,4-dihydro-2H-3-oxa-1,8-diaza-naphthalene;

5-(1-ethyl-propoxy)-7-methyl-1-(2,6-dimethyl-4-chloro-phenyl)-1,2-dihydro-3-oxa-1,8-diaza-naphthalen-4-one;

8-(1-ethyl-propoxy)-1,6-dimethyl-4-(2,6-dimethyl-4-chloro-phenyl)-1,2,3,4-tetrahydro-pyrido[2,3-b]pyrazine;

20 (1-ethyl-propyl)-[2-methyl-8-(2,6-dimethyl-4-chloro-phenyl)-quinolin-4-yl]-amine;

8-(1-hydroxymethyl-propoxy)-6-methyl-4-(2,4,6-trimethyl-phenyl)-3,4-dihydro-1H-pyrido[2,3-b]pyrazin-2-one;

8-(1-hydroxymethyl-propylamino)-6-methyl-4-(2,4,6-trimethyl-phenyl)-3,4-dihydro-1H-pyrido[2,3-b]pyrazin-2-one;

25 8-(1-ethyl-propylamino)-6-methyl-4-(2,4,6-trimethyl-phenyl)-3,4-dihydro-1H-pyrido[2,3-b]pyrazin-2-one;

8-diethylamino-6-methyl-4-(2,4,6-trimethyl-phenyl)-3,4-dihydro-1H-pyrido-[2,3-b] pyrazin-2-one;

30 8-(ethyl-propyl-amino)-6-methyl-4-(2,4,6-trimethyl-phenyl)-3,4-dihydro-1H-pyrido[2,3-b]pyrazin-2-one;

8-(butyl-ethyl-amino)-6-methyl-4-(2,4,6-trimethyl-phenyl)-3,4-dihydro-1H-pyrido [2,3-b]pyrazin-2-one;

8-(1-hydroxymethyl-propoxy)-6-methyl-4-(2,4,6-trimethyl-phenyl)-1,2,3,4-tetrahydro-pyrido[2,3-b]pyrazine;

8-(1-hydroxymethyl-propylamino)-6-methyl-4-(2,4,6-trimethyl-phenyl)-1,2,3,4-tetrahydro-pyrido[2,3-b]pyrazine;

5 8-(1-ethyl-propylamino)-6-methyl-4-(2,4,6-trimethyl-phenyl)-1,2,3,4-tetrahydro-pyrido[2,3-b]pyrazine;

8-diethylamino-6-methyl-4-(2,4,6-trimethyl-phenyl)-1,2,3,4-tetrahydro-pyrido[2,3-b]pyrazine;

8-(ethyl-propyl-amino)-6-methyl-4-(2,4,6-trimethyl-phenyl)-1,2,3,4-tetrahydro-10 pyrido[2,3-b]pyrazine;

8-(butyl-ethyl-amino)-6-methyl-4-(2,4,6-trimethyl-phenyl)-1,2,3,4-tetrahydro-pyrido[2,3-b]pyrazine;

4-(1-hydroxymethyl-propoxy)-2-methyl-8-(2,4,6-trimethyl-phenyl)-quinoline;

4-(1-hydroxymethyl-propylamino)-2-methyl-8-(2,4,6-trimethyl-phenyl)-15 quinoline;

4-(1-ethyl-propylamino)-2-methyl-8-(2,4,6-trimethyl-phenyl)-quinoline;

4-(butyl-ethyl-amino)-2-methyl-8-(2,4,6-trimethyl-phenyl)-quinoline;

20 5-(1-hydroxymethyl-propoxy)-7-methyl-1-(2,4,6-trimethyl-phenyl)-1,4-dihydro-2H-3-oxa-1,8-diaza-naphthalene;

5-(1-hydroxymethyl-propylamino)-7-methyl-1-(2,4,6-trimethyl-phenyl)-1,4-dihydro-2H-3-oxa-1,8-diaza-naphthalene;

5-(1-ethyl-propylamino)-7-methyl-1-(2,4,6-trimethyl-phenyl)-1,4-dihydro-2H-3-25 oxa-1,8-diaza-naphthalene;

5-diethylamino-5-methyl-1-(2,4,6-trimethyl-phenyl)-1,4-dihydro-2H-3-oxa-1,8-diaza-naphthalene;

5-(ethyl-propyl-amino)-7-methyl-1-(2,4,6-trimethyl-phenyl)-1,4-dihydro-2H-3-oxa-1,8-diaza-naphthalene;

30 8-(butyl-ethyl-amino)-6-methyl-4-(2,4,6-trimethyl-phenyl)-1,4-dihydro-2H-3-oxa-1,8-diaza-naphthalene;

4-(2,4-dichlorophenyl)-5-methyl-2-[N-(1-(methoxymethyl)-1-(naphth-2-yl)methyl)-N-propylamino]thiazole;

oxalate of 4-(2,4-dichlorophenyl)-5-methyl-2-[N-(6-methoxyisoquinol-5-yl)-N-propylamino]thiazole;

oxalate of 4-(2-chloro-4-methoxyphenyl)-5-methyl-2-[N-(6-methoxyisoquinol-5-yl)-N-propylamino]thiazole;

5 4-(2-chloro-4-methoxyphenyl)-5-methyl-2-[N-(1-methoxycarbonylmethylindol-5-yl)-N-propylamino]thiazole;

oxalate of 4-(2-chloro-4-methoxyphenyl)-5-methyl-2-[N-(6-methoxyisoquinol-5-yl)-N-propylamino]thiazole;

oxalate of 4-(2-chloro-4-methoxyphenyl)-5-methyl-2-[N-(6-chloroisoquinol-5-yl)-N-propylamino]thiazole;

10 oxalate of 4-(2-chloro-4-methoxyphenyl)-5-methyl-2-[N-(6-methoxyisoquinol-5-yl)-N-propylamino]thiazole;

oxalate of 4-(2-chloro-4-methoxyphenyl)-5-methyl-2-[N-(6-methoxyisoquinol-5-yl)-N-propylamino]thiazole;

4-(2-chloro-4-methoxyphenyl)-5-methyl-2-[N-1-methoxynaphth-2-yl)-N-propylamino]thiazole;

15 oxalate of 4-(2-chloro-4-trifluoromethylphenyl)-5-methyl-2-[N-6-methoxyisoquinol-5-yl)-N-propylamino]thiazole;

chlorhydrate of 4-(2-chloro-4-methoxyphenyl)-5-methyl-2-[N-(2-ethoxynaphth-1-yl)-N-propylamino]thiazole;

chlorhydrate of 4-(2-chloro-4-methoxyphenyl)-5-methyl-2-[N-(2,3-dimethylnaphth-1-yl)-N-propylamino]thiazole;

20 chlorhydrate of 4-(2-chloro-4-methoxyphenyl)-5-methyl-2-[N-(6-bromo-2-methoxynaphth-1-yl)-N-propylamino]thiazole;

chlorhydrate of 4-(2-chloro-4-methoxyphenyl)-5-methyl-2-[N-(2,6-dimethylnaphth-1-yl)-N-propylamino]thiazole;

25 chlorhydrate of 4-(2-chloro-4-methoxyphenyl)-5-methyl-2-[N-(1-(methoxymethyl)-1-(naphth-2-yl)methyl)-N-propylamino]thiazole;

chlorhydrate of 4-(2-chloro-4-methoxyphenyl)-5-methyl-2-[N-(1-(cyclopropyl)-1-(naphth-2-yl)methyl)-N-propylamino]thiazole;

30 3-(2,4-dichlorophenyl)-5-methyl-7(N-propyl-N-cyclopropanemethylamino)-pyrazolo[2,3-a]pyrimidine;

3-(2,4-dichlorophenyl)-5-methyl-7-(N-allyl-N-cyclopropanemethylamino)-pyrazolo[2,3-a]pyrimidine;

2-methylthio-3-(2,4-dichlorophenyl)-5-methyl-7-(N,N-diallylamino)-pyrazolo[2,3-a]pyrimidine;

2-methylthio-3-(2,4-dichlorophenyl)-5-methyl-7-(N-butyl-N-cyclopropane-methyl-amino)pyrazolo[2,3-a]pyrimidine;

2-methylthio-3-(2,4-dichlorophenyl)-5-methyl-7-(N-propyl-N-cyclopropane-methyl-amino)pyrazolo[2,3-a]pyrimidine;

5 2-methyl-3-(4-chlorophenyl)-5-methyl-7-(N,N-dipropylamino)-pyrazolo[2,3-a]pyrimidine;

3-[6-(dimethylamino)-3-pyridinyl-2,5-dimethyl-N,N-dipropylpyrazolo[2,3-a]pyrimidin-7-amine;

3-[6-(dimethylamino)-4-methyl-3-pyridinyl]-2,5-dimethyl-N,N-dipropyl-10 pyrazolo[2,3-a]pyrimidine-7-amine;

3-(2,4-dimethoxyphenyl)-2,5-dimethyl-7-(N-propyl-N-methoxyethylamino)-pyrazolo(2,3-a)pyrimidine;

7-(N-diethylamino)-2,5-dimethyl-3-(2-methyl-4-methoxyphenyl-[1,5-a]-pyrazolopyrimidine;

15 7-(N-(3-cyanopropyl)-N-propylamino-2,5,dimethyl-3-(2,4-dimethylphenyl)-[1,5-a]-pyrazolopyrimidine;

[3,6-dimethyl-2-(2,4,6-trimethyl-phenoxy)-pyridin-4-yl]-(1-ethyl-propyl)-amine;

[2-(4-chloro-2,6-dimethyl-phenoxy)-3,6-dimethyl-pyridin-4-yl]-(1-ethyl-propyl)-amine;

20 cyclopropylmethyl-[3-(2,4-dimethyl-phenyl)-2,5-dimethyl-pyrazolo[1,5-a]pyrimidin-7-yl]-propyl-amine;

cyclopropylmethyl-[3-(2-methyl-4-chloro-phenyl)-2,5-dimethyl-pyrazolo[1,5-a]pyrimidin-7-yl]-propyl-amine;

cyclopropylmethyl-[3-(2,4-di-chloro-phenyl)-2,5-dimethyl-pyrazolo[1,5-a]pyrimidin-7-yl]-propyl-amine;

25 [3-(2-methyl-4-chloro-phenyl)-2,5-dimethyl-pyrazolo[1,5-a]pyrimidin-7-yl]-di-propyl-amine;

[2,5-dimethyl-3-(2,4-dimethyl-phenyl)-pyrazolo[1,5-a]pyrimidin-7-yl]-(1-ethyl-propyl)-amine;

30 [2,5-dimethyl-3-(2,4-dichloro-phenyl)-pyrazolo[1,5-a]pyrimidin-7-yl]-(1-ethyl-propyl)-amine;

4-(1-ethyl-propylamino)-6-methyl-2-(2,4,6-trimethyl-phenoxy)-nicotinic acid methyl ester;

3-[6-(dimethylamino)-4-methyl-3-pyridinyl]-2,5-dimethyl-N-propyl-N-cyclopropylmethyl-pyrazolo[2,3-a]pyrimidin-7-amine; and

3-[6-(dimethylamino)-4-methyl-3-pyridinyl]-2,5-dimethyl-N-ethyl-N-cyclopropylmethyl-pyrazolo[2,3-a]pyrimidin-7-amine.

5

14. A pharmaceutical composition according to claim 13 wherein said corticotropin releasing factor antagonist is a compound selected from the group consisting of:

4-(1-ethyl-propoxy)-3,6-dimethyl-2-(2,4,6-trimethylphenoxy)-pyridine;

10 4-(1-ethylpropoxy)-2,5-dimethyl-6-(2,4,6-trimethylphenoxy)-pyrimidine;

[4-(1-ethyl-propoxy)-3,6-dimethyl-pyridin-2-yl]-(2,4,6-trimethylphenyl)-amine;

3-{(4-methyl-benzyl)-[3,6-dimethyl-1-(2,4,6-trimethylphenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yl]-amino}-propan-1-ol;

propyl-ethyl-[3,6-dimethyl-1-(2,4,6-trimethylphenyl)-1H-pyrazolo[3,4-15 d]pyrimidin-4-yl]-amine;

ethyl-n-propyl-[2,5-dimethyl-7-(2,4,6-trimethylphenyl)-7H-pyrrolo[2,3-d]pyrimidin-4-yl]amine;

2-{N-n-butyl-N-[2,5-dimethyl-7-(2,4,6-trimethylphenyl)-7H-pyrrolo[2,3-d]pyrimidin-4-yl]amino}-ethanol;

20 [3,6-dimethyl-1-(2,4,6-trimethylphenyl)-1H-pyrazolo[3,4,b]pyridin-4-yl]-(1-methoxymethylpropyl)-amine;

4-(1-ethylpropoxy)-2,5-dimethyl-7-(2,4,6-trimethylphenyl)-7H-pyrrolo[2,3-b]pyridine;

25 2,5,6-trimethyl-7-(1-propylbutyl)-4-(2,4,6-trimethylphenoxy)-7H-pyrrolo[2,3-d]pyrimidine;

1-(1-ethylpropyl)-6-methyl-4-(2,4,6-trimethylphenoxy)-1,3-dihydro-imidazo[4,5-c]pyridin-2-one;

1-(1-ethyl-propyl)-4,7-dimethyl-5-(2,4,6-trimethyl-phenoxy)-1,4-dihydro-2H-pyrido[3,4-b]pyrazin-3-one;

30 1-(1-ethyl-propyl)-4,7-dimethyl-5-(2,4,6-trimethyl-phenoxy)-1,2,3,4-tetrahydro-pyrido[3,4-b]pyrazine;

1-(1-ethyl-propyl)-7-methyl-2-oxo-5-(2,4,6-trimethyl-phenoxy)-1,2,3,4-tetrahydro-[1,6]naphthyridine-3-carboxylic acid isopropyl ester;

1-(1-ethyl-propyl)-7-methyl-5-(2,4,6-trimethyl-phenoxy)-1,4-dihydro-2H-3-oxa-1,6-diaza-naphthalene;

(1-ethyl-propyl)-[5-methyl-3-(2,4,6-trimethyl-phenyl)-pyrazolo[1,5-a]pyrimidin-7-yl]-amine;

5 7-(1-ethyl-propoxy)-2,5-dimethyl-3-(2,4,6-trimethyl-phenyl)-pyrazolo[1,5-a]pyrimidine;

4-(1-ethyl-propoxy)-2,5-dimethyl-7-(2,4,6-trimethyl-phenyl)-5H-pyrrolo[3,2-d]pyrimidine;

4-(butyl-ethyl-amino)-2,6-dimethyl-8-(2,4,6-trimethyl-phenyl)-5,8-dihydro-6H-10 pyrido[2,3-d]pyrimidin-7-one;

8-(1-ethyl-propoxy)-6-methyl-4-(2,4,6-trimethyl-phenyl)-1,2,3,4-tetrahydro-pyrido [2,3-b]pyrazine;

4-(1-ethyl-propoxy)-2-methyl-8-(2,4,6-trimethyl-phenyl)-quinoline;

(1-ethyl-propyl)-[2-methyl-8-(2,4,6-trimethyl-phenyl)-quinolin-4-yl]-amine;

15 (propyl-ethyl)-[2-methyl-8-(2,4,6-trimethyl-phenyl)-5,6,7,8-tetrahydro-pyrido-[2,3-d] pyrimidin-4-yl]-amine;

(1-ethyl-propoxy)-2-methyl-8-(2,4,6-trimethyl-phenyl)-5,6,7,8-tetrahydro-pyrido[2,3-d] pyrimidine;

8-(1-hydroxymethyl-propylamino)-6-methyl-4-(2,4,6-trimethyl-phenyl)-3,4-20 dihydro-1H-pyrido[2,3-b]pyrazin-2-one;

4-(1-hydroxymethyl-propylamino)-2-methyl-8-(2,4,6-trimethyl-phenyl)-quinoline;

5-(1-hydroxymethyl-propylamino)-7-methyl-1-(2,4,6-trimethyl-phenyl)-1,4-dihydro-2H-3-oxa-1,8-diaza-naphthalene;

25 [3,6-dimethyl-2-(2,4,6-trimethyl-phenoxy)-pyridin-4-yl]- (1-ethyl-propyl)-amine; cyclopropylmethyl-[3-(2,4-dimethyl-phenyl)-2,5-dimethyl-pyrazolo[1,5-a]pyrimidin-7-yl]-propyl-amine;

[2,5-dimethyl-3-(2,4-dimethyl-phenyl)-pyrazolo[1,5-a]pyrimidin-7-yl]- (1-ethyl-propyl)-amine;

30 3-[6-(dimethylamino)-3-pyridinyl-2,5-dimethyl-N,N-dipropylpyrazolo[2,3-a]pyrimidin-7-amine;

3-[6-(dimethylamino)-4-methyl-3-pyridinyl]-2,5-dimethyl-N,N-dipropyl-pyrazolo[2,3-a]pyrimidine-7-amine;

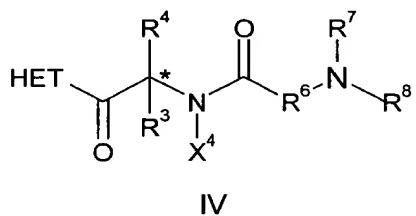
3-(2,4-dimethoxyphenyl)-2,5-dimethyl-7-(N-propyl-N-methyloxyethylamino)-pyrazolo(2,3-a)pyrimidine;

7-(N-diethylamino)-2,5-dimethyl-3-(2-methyl-4-methoxyphenyl-[1,5-a]-pyrazolopyrimidine; and

5 7-(N-(3-cyanopropyl)-N-propylamino-2,5-dimethyl-3-(2,4-dimethylphenyl)-[1,5-a]-pyrazolopyrimidine.

15. A pharmaceutical composition according to claim 1 wherein said growth hormone secretagogue is a compound of formula IV:

10

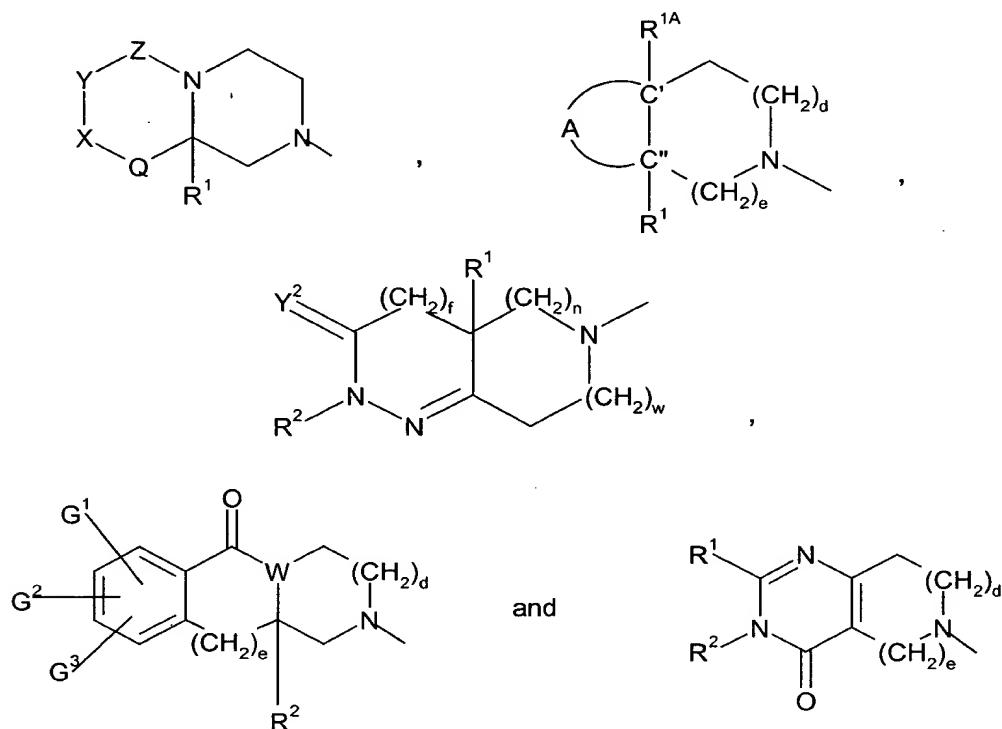


IV

or a stereoisomeric mixture thereof, a diastereomerically enriched, diastereomerically pure, enantiomerically enriched, or enantiomerically pure isomer thereof, or a prodrug of such compound, mixture, or isomer thereof, or a pharmaceutically acceptable salt

15 of the compound, mixture, isomer, or prodrug, wherein:

HET is a heterocyclic moiety selected from the group consisting of



$d$  is 0, 1, or 2;

e is 1 or 2;

f is 0 or 1;

5 n and w are 0, 1, or 2, provided that n and w cannot both be 0 at the same time;

$Y^2$  is oxygen or sulfur;

A is a divalent radical, wherein the left hand side of the radical as shown below is connected to C" and the right hand side of the radical as shown below is connected to C', selected from the group consisting of  $-\text{NR}^2\text{-CO-NR}^2$ -,  $-\text{NR}^2\text{-SO}_2\text{-NR}^2$ -,  $-\text{O-CO-NR}^2$ -,  $-\text{NR}^2\text{-CO}_2$ -,  $-\text{CO-NR}^2\text{-CO}$ -,  $-\text{CO-NR}^2\text{-C(R}^9\text{R}^{10}\text{)}$ -,  $-\text{C(R}^9\text{R}^{10}\text{)-NR}^2\text{-CO}$ -,  $-\text{C(R}^9\text{R}^{10}\text{)-C(R}^9\text{R}^{10}\text{)-C(R}^9\text{R}^{10}\text{)}$ -,  $-\text{SO}_2\text{-C(R}^9\text{R}^{10}\text{)-C(R}^9\text{R}^{10}\text{)}$ -,  $-\text{C(R}^9\text{R}^{10}\text{)-O-CO}$ -,  $-\text{C(R}^9\text{R}^{10}\text{)-O-C(R}^9\text{R}^{10}\text{)}$ -,  $-\text{NR}^2\text{-CO-C(R}^9\text{R}^{10}\text{)}$ -,  $-\text{O-CO-C(R}^9\text{R}^{10}\text{)}$ -,  $-\text{C(R}^9\text{R}^{10}\text{)-CO-NR}^2$ -,  $-\text{CO-NR}^2\text{-CO}$ -,  $-\text{C(R}^9\text{R}^{10}\text{)-CO}_2$ -,  $-\text{CO-NR}^2\text{-C(R}^9\text{R}^{10}\text{)-C(R}^9\text{R}^{10}\text{)}$ -,  $-\text{CO}_2\text{-C(R}^9\text{R}^{10}\text{)}$ -,  $-\text{C(R}^9\text{R}^{10}\text{)-C(R}^9\text{R}^{10}\text{)-C(R}^9\text{R}^{10}\text{)-C(R}^9\text{R}^{10}\text{)}$ -,  $-\text{SO}_2\text{-NR}^2\text{-C(R}^9\text{R}^{10}\text{)}$ -,  $-\text{C(R}^9\text{R}^{10}\text{)-C(R}^9\text{R}^{10}\text{)-NR}^2\text{-CO}$ -,  $-\text{C(R}^9\text{R}^{10}\text{)-C(R}^9\text{R}^{10}\text{)-O-CO}$ -,  $-\text{NR}^2\text{-CO-C(R}^9\text{R}^{10}\text{)-C(R}^9\text{R}^{10}\text{)}$ -,  $-\text{NR}^2\text{-SO}_2\text{-C(R}^9\text{R}^{10}\text{)-C(R}^9\text{R}^{10}\text{)}$ -,  $-\text{O-CO-C(R}^9\text{R}^{10}\text{)-C(R}^9\text{R}^{10}\text{)}$ -,  $-\text{C(R}^9\text{R}^{10}\text{)-C(R}^9\text{R}^{10}\text{)-CO-NR}^2$ -,  $-\text{C(R}^9\text{R}^{10}\text{)-C(R}^9\text{R}^{10}\text{)-CO}$ -,  $-\text{C(R}^9\text{R}^{10}\text{)-NR}^2\text{-CO}_2$ -,  $-\text{C(R}^9\text{R}^{10}\text{)-O-CO-NR}^2$ -,  $-\text{C(R}^9\text{R}^{10}\text{)-NR}^2\text{-CO-NR}^2$ -,  $-\text{NR}^2\text{-CO}_2\text{-C(R}^9\text{R}^{10}\text{)}$ -,  $-\text{NR}^2\text{-CO-NR}^2$ -.

$C(R^9R^{10})$ - $, -NR^2-SO_2-NR^2-C(R^9R^{10})$ - $, -O-CO-NR^2-C(R^9R^{10})$ - $, -CO-N=C(R^{11})-NR^2$ - $, -CO-NR^2-C(R^{11})=N$ - $, -C(R^9R^{10})-NR^{12}-C(R^9R^{10})$ - $, -NR^{12}-C(R^9R^{10})$ - $, -C(R^9R^{10})$ - $, -CO_2-C(R^9R^{10})-C(R^9R^{10})$ - $, -NR^2-C(R^{11})=N-CO$ - $, -C(R^9R^{10})-C(R^9R^{10})-N(R^{12})$ - $, -C(R^9R^{10})-NR^{12}$ - $, -N=C(R^{11})-NR^2-CO$ - $, -C(R^9R^{10})-C(R^9R^{10})-NR^2-SO_2$ - $, -C(R^9R^{10})$ -  
5  $C(R^9R^{10})-SO_2-NR^2$ - $, -C(R^9R^{10})-C(R^9R^{10})-CO_2$ - $, -C(R^9R^{10})-SO_2-C(R^9R^{10})$ - $, -C(R^9R^{10})$ - $C(R^9R^{10})-SO_2$ - $, -O-C(R^9R^{10})-C(R^9R^{10})$ - $, -C(R^9R^{10})-C(R^9R^{10})-O$ - $, -C(R^9R^{10})-CO$ - $C(R^9R^{10})$ - $, -CO-C(R^9R^{10})-C(R^9R^{10})$ - $, \text{and } -C(R^9R^{10})-NR^2-SO_2-NR^2$ -;

Q is a covalent bond or  $CH_2$ ;

W is CH or N;

10 X is  $CR^9R^{10}$ ,  $C=CH_2$ , or  $C=O$ ;

Y is  $CR^9R^{10}$ , O, or  $NR^2$ ;

Z is  $C=O$ ,  $C=S$ , or  $SO_2$ ;

$G^1$  is hydrogen, halo, hydroxy, nitro, amino, cyano, phenyl, carboxyl,  $-CONH_2$ ,  $-C_1-C_4$  alkyl optionally independently substituted with one or more phenyl, one or more halogen, or one or more hydroxy groups,  $-C_1-C_4$  alkoxy optionally independently substituted with one or more phenyl, one or more halogen, or one or more hydroxy groups,  $-C_1-C_4$  alkylthio, phenoxy,  $-CO_2-(C_1-C_4 \text{ alkyl})$ ,  $N,N$ -di( $C_1-C_4$  alkylamino),  $-C_2-C_6$  alkenyl optionally independently substituted with one or more phenyl, one or more halogen, or one or more hydroxy groups,  $-C_2-C_6$  alkynyl optionally independently substituted with one or more phenyl, one or more halogen, or one or more hydroxy groups,  $-C_3-C_6$  cycloalkyl optionally independently substituted with one or more  $C_1-C_4$  alkyl groups, one or more halogen, or one or more hydroxy groups,  $-C_1-C_4$  alkylamino carbonyl, or di- $C_1-C_4$  alkylamino carbonyl;

25  $G^2$  and  $G^3$  are each independently selected from the group consisting of hydrogen, halo, hydroxy,  $-C_1-C_4$  alkyl optionally independently substituted with one to three halo groups, and  $-C_1-C_4$  alkoxy optionally independently substituted with one to three halo groups;

$R^1$  is hydrogen,  $-CN$ ,  $-(CH_2)_qNX^6COX^6$ ,  $-(CH_2)_qNX^6CO(CH_2)_t-A^1$ ,  $-(CH_2)_qNX^6SO_2(CH_2)_t-A^1$ ,  $-(CH_2)_qNX^6SO_2X^6$ ,  $-(CH_2)_qNX^6CONX^6(CH_2)_t-A^1$ ,  $-(CH_2)_qNX^6CONX^6X^6$ ,  $-(CH_2)_qCONX^6X^6$ ,  $-(CH_2)_qCONX^6(CH_2)_t-A^1$ ,  $-(CH_2)_qCO_2X^6$ ,  $-(CH_2)_qCO_2(CH_2)_t-A^1$ ,  $-(CH_2)_qOX^6$ ,  $-(CH_2)_qOCOX^6$ ,  $-(CH_2)_qOCO(CH_2)_t-A^1$ ,  $-(CH_2)_qOCONX^6(CH_2)_t-A^1$ ,  $-(CH_2)_qOCONX^6X^6$ ,  $-(CH_2)_qCOX^6$ ,  $-(CH_2)_qCO(CH_2)_t-A^1$ ,  $-(CH_2)_qNX^6CO_2X^6$ ,  $-(CH_2)_qNX^6SO_2NX^6X^6$ ,  $-(CH_2)_qSO_mX^6$ ,  $-(CH_2)_qSO_m(CH_2)_t-A^1$ ,

-C<sub>1</sub>-C<sub>10</sub> alkyl, -(CH<sub>2</sub>)<sub>t</sub>-A<sup>1</sup>, -(CH<sub>2</sub>)<sub>q</sub>-(C<sub>3</sub>-C<sub>7</sub> cycloalkyl), -(CH<sub>2</sub>)<sub>q</sub>-Y<sup>1</sup>-(C<sub>1</sub>-C<sub>6</sub> alkyl), -(CH<sub>2</sub>)<sub>q</sub>-Y<sup>1</sup>-(CH<sub>2</sub>)<sub>t</sub>-A<sup>1</sup>, or -(CH<sub>2</sub>)<sub>q</sub>-Y<sup>1</sup>-(CH<sub>2</sub>)<sub>t</sub>-(C<sub>3</sub>-C<sub>7</sub> cycloalkyl);

5           wherein the alkyl and cycloalkyl groups in the definition of R<sup>1</sup> are optionally substituted with C<sub>1</sub>-C<sub>4</sub> alkyl, hydroxy, C<sub>1</sub>-C<sub>4</sub> alkoxy, carboxyl, -CONH<sub>2</sub>, -SO<sub>m</sub>-(C<sub>1</sub>-C<sub>6</sub> alkyl), -CO<sub>2</sub>-(C<sub>1</sub>-C<sub>4</sub> alkyl) ester, 1H-tetrazol-5-yl, or 1, 2, or 3 fluoro groups;

10           Y<sup>1</sup> is O, SO<sub>m</sub>, -CONX<sup>6</sup>-, -CH=CH-, -C≡C-, -NX<sup>6</sup>CO-, -CONX<sup>6</sup>-, -CO<sub>2</sub>-, -OCONX<sup>6</sup>- or -OCO-;

10           q is 0, 1, 2, 3, or 4;

10           t is 0, 1, 2, or 3;

10           said (CH<sub>2</sub>)<sub>q</sub> group and (CH<sub>2</sub>)<sub>t</sub> group in the definition of R<sup>1</sup> are optionally independently substituted with hydroxy, C<sub>1</sub>-C<sub>4</sub> alkoxy, carboxyl, -CONH<sub>2</sub>, -SO<sub>m</sub>-(C<sub>1</sub>-C<sub>6</sub> alkyl), -CO<sub>2</sub>-(C<sub>1</sub>-C<sub>4</sub> alkyl) ester, 1H-tetrazol-5-yl, 1, 2, or 3 fluoro groups, or 1 or 2 C<sub>1</sub>-C<sub>4</sub> alkyl groups;

15           R<sup>1A</sup> is selected from the group consisting of hydrogen, F, Cl, Br, I, C<sub>1</sub>-C<sub>6</sub> alkyl, phenyl-(C<sub>1</sub>-C<sub>3</sub> alkyl), pyridyl-(C<sub>1</sub>-C<sub>3</sub> alkyl), thiazolyl-(C<sub>1</sub>-C<sub>3</sub> alkyl), and thieryl-(C<sub>1</sub>-C<sub>3</sub> alkyl), provided that R<sup>1A</sup> is not F, Cl, Br, or I when a heteroatom is vicinal to C";

20           R<sup>2</sup> is hydrogen, C<sub>1</sub>-C<sub>8</sub> alkyl, -(C<sub>0</sub>-C<sub>3</sub> alkyl)-(C<sub>3</sub>-C<sub>8</sub> cycloalkyl), -(C<sub>1</sub>-C<sub>4</sub> alkyl)-A<sup>1</sup>, or A<sup>1</sup>, wherein the alkyl groups and the cycloalkyl groups in the definition of R<sup>2</sup> are optionally substituted with hydroxy, -CO<sub>2</sub>X<sup>6</sup>, -CONX<sup>6</sup>X<sup>6</sup>, -NX<sup>6</sup>X<sup>6</sup>, -SO<sub>m</sub>(C<sub>1</sub>-C<sub>6</sub> alkyl), -COA<sup>1</sup>, -COX<sup>6</sup>, CF<sub>3</sub>, CN, or 1, 2, or 3 independently selected halo groups;

25           R<sup>3</sup> is selected from the group consisting of A<sup>1</sup>, C<sub>1</sub>-C<sub>10</sub> alkyl, -(C<sub>1</sub>-C<sub>6</sub> alkyl)-A<sup>1</sup>, -(C<sub>1</sub>-C<sub>6</sub> alkyl)-(C<sub>3</sub>-C<sub>7</sub> cycloalkyl), -(C<sub>1</sub>-C<sub>5</sub> alkyl)-X<sup>1</sup>-(C<sub>1</sub>-C<sub>5</sub> alkyl), -(C<sub>1</sub>-C<sub>5</sub> alkyl)-X<sup>1</sup>-(C<sub>0</sub>-C<sub>5</sub> alkyl)-A<sup>1</sup>, and -(C<sub>1</sub>-C<sub>5</sub> alkyl)-X<sup>1</sup>-(C<sub>1</sub>-C<sub>5</sub> alkyl)-(C<sub>3</sub>-C<sub>7</sub> cycloalkyl);

25           wherein the alkyl groups in the definition of R<sup>3</sup> are optionally substituted with -SO<sub>m</sub>(C<sub>1</sub>-C<sub>6</sub> alkyl), -CO<sub>2</sub>X<sup>3</sup>, 1, 2, 3, 4, or 5 independently selected halo groups, or 1, 2, or 3 independently selected -OX<sup>3</sup> groups;

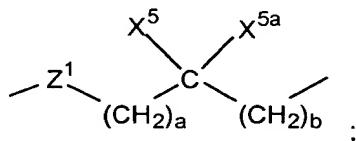
30           X<sup>1</sup> is O, SO<sub>m</sub>, -NX<sup>2</sup>CO-, -CONX<sup>2</sup>-, -OCO-, -CO<sub>2</sub>-, -CX<sup>2</sup>=CX<sup>2</sup>-, -NX<sup>2</sup>CO<sub>2</sub>-, -OCONX<sup>2</sup>-, or -C≡C-;

30           R<sup>4</sup> is hydrogen, C<sub>1</sub>-C<sub>6</sub> alkyl, or C<sub>3</sub>-C<sub>7</sub> cycloalkyl, or R<sup>4</sup> taken together with R<sup>3</sup> and the carbon atom to which they are attached form C<sub>5</sub>-C<sub>7</sub> cycloalkyl, C<sub>5</sub>-C<sub>7</sub> cycloalkenyl, a partially saturated or fully saturated 4- to 8-membered ring having 1 to 4 heteroatoms independently selected from the group consisting of oxygen, sulfur, and nitrogen, or a bicyclic ring system consisting of a partially saturated or fully

saturated 5- or 6-membered ring, fused to a partially saturated, fully unsaturated, or fully saturated 5- or 6-membered ring, optionally having 1 to 4 heteroatoms independently selected from the group consisting of nitrogen, sulfur, and oxygen;

5       $X^4$  is hydrogen or  $C_1-C_6$  alkyl, or  $X^4$  is taken together with  $R^4$  and the nitrogen atom to which  $X^4$  is attached and the carbon atom to which  $R^4$  is attached and form a five to seven membered ring;

$R^6$  is a bond or is



10      wherein a and b are each independently 0, 1, 2, or 3;

10       $X^5$  and  $X^{5a}$  are each independently selected from the group consisting of hydrogen,  $CF_3$ ,  $A^1$ , and  $C_1-C_6$  alkyl optionally substituted with  $A^1$ ,  $OX^2$ ,  $-SO_m-(C_1-C_6$  alkyl),  $-CO_2X^2$ ,  $C_3-C_7$  cycloalkyl,  $-NX^2X^2$ , or  $-CONX^2X^2$ ;

15      or the carbon bearing  $X^5$  or  $X^{5a}$  forms one or two alkylene bridges with the nitrogen atom bearing  $R^7$  and  $R^8$  wherein each alkylene bridge contains 1 to 5 carbon atoms, provided that when one alkylene bridge is formed then only one of  $X^5$  or  $X^{5a}$  is on the carbon atom and only one of  $R^7$  or  $R^8$  is on the nitrogen atom, and further provided that when two alkylene bridges are formed then  $X^5$  and  $X^{5a}$  cannot be on the carbon atom and  $R^7$  and  $R^8$  cannot be on the nitrogen atom;

20      or  $X^5$  taken together with  $X^{5a}$  and the carbon atom to which they are attached form a partially saturated or fully saturated 3- to 7-membered ring, or a partially saturated or fully saturated 4- to 8-membered ring having 1 to 4 heteroatoms independently selected from the group consisting of oxygen, sulfur, and nitrogen;

25      or  $X^5$  taken together with  $X^{5a}$  and the carbon atom to which they are attached form a bicyclic ring system consisting of a partially saturated or fully saturated 5- or 6-membered ring, optionally having 1 or 2 heteroatoms independently selected from the group consisting of nitrogen, sulfur, and oxygen, fused to a partially saturated, fully saturated, or fully unsaturated 5- or

6-membered ring, optionally having 1 to 4 heteroatoms independently selected from the group consisting of nitrogen, sulfur, and oxygen;

$Z^1$  is a bond, O, or  $N-X^2$ , provided that when a and b are both 0 then  $Z^1$  is not  $N-X^2$  or O;

5  $R^7$  and  $R^8$  are each independently hydrogen or  $C_1-C_6$  alkyl optionally independently substituted with  $A^1$ ,  $-CO_2-(C_1-C_6$  alkyl),  $-SO_m(C_1-C_6$  alkyl), 1 to 5 halo groups, 1 to 3 hydroxy groups, 1 to 3  $-O-CO(C_1-C_{10}$  alkyl) groups, or 1 to 3  $C_1-C_6$  alkoxy groups; or

10  $R^7$  and  $R^8$  can be taken together to form  $-(CH_2)_r-L-(CH_2)_r$ , wherein L is  $CX^2X^2$ ,  $SO_m$ , or  $NX^2$ ;

$R^9$  and  $R^{10}$  are each independently selected from the group consisting of hydrogen, fluoro, hydroxy, and  $C_1-C_5$  alkyl optionally independently substituted with 1-5 halo groups;

15  $R^{11}$  is selected from the group consisting of  $C_1-C_5$  alkyl and phenyl optionally substituted with 1-3 substituents each independently selected from the group consisting of  $C_1-C_5$  alkyl, halo, and  $C_1-C_5$  alkoxy;

20  $R^{12}$  is selected from the group consisting of  $C_1-C_5$  alkylsulfonyl,  $C_1-C_5$  alkanoyl, and  $C_1-C_5$  alkyl wherein the alkyl portion is optionally independently substituted by 1-5 halo groups;

25  $A^1$  for each occurrence is independently selected from the group consisting of  $C_5-C_7$  cycloalkenyl, phenyl, a partially saturated, fully saturated, or fully unsaturated 4- to 8-membered ring optionally having 1 to 4 heteroatoms independently selected from the group consisting of oxygen, sulfur, and nitrogen, and a bicyclic ring system consisting of a partially saturated, fully unsaturated, or fully saturated 5- or 6-membered ring, optionally having 1 to 4 heteroatoms independently selected from the group consisting of nitrogen, sulfur, and oxygen, fused to a partially saturated, fully saturated, or fully unsaturated 5- or 6-membered ring, optionally having 1 to 4 heteroatoms independently selected from the group consisting of nitrogen, sulfur, and oxygen;

30  $A^1$  for each occurrence is independently optionally substituted, on one or optionally both rings if  $A^1$  is a bicyclic ring system, with up to three substituents, each substituent independently selected from the group consisting of F, Cl, Br, I,  $OCF_3$ ,  $OCF_2H$ ,  $CF_3$ ,  $CH_3$ ,  $OCH_3$ ,  $-OX^6$ ,  $-CONX^6X^6$ ,  $-CO_2X^6$ , oxo,  $C_1-C_6$  alkyl, nitro, cyano, benzyl,  $-SO_m(C_1-C_6$  alkyl), 1H-tetrazol-5-

yl, phenyl, phenoxy, phenylalkyloxy, halophenyl, methylenedioxy,  $-NX^6X^6$ ,  $-NX^6COX^6$ ,  $-SO_2NX^6X^6$ ,  $-NX^6SO_2$ -phenyl,  $NX^6SO_2X^6$ ,  $-CONX^{11}X^{12}$ ,  $-SO_2NX^{11}X^{12}$ ,  $-NX^6SO_2X^{12}$ ,  $-NX^6CONX^{11}X^{12}$ ,  $-NX^6SO_2NX^{11}X^{12}$ ,  $-NX^6COX^{12}$ , imidazolyl, thiazolyl, and tetrazolyl, provided that if  $A^1$  is optionally substituted with methylenedioxy then it can only be substituted with one methylenedioxy;

5

wherein  $X^{11}$  is hydrogen or  $C_1$ - $C_6$  alkyl optionally independently substituted with phenyl, phenoxy,  $C_1$ - $C_6$  alkoxy carbonyl,  $-SO_m(C_1$ - $C_6$  alkyl), 1 to 5 halo groups, 1 to 3 hydroxy groups, 1 to 3  $C_1$ - $C_{10}$  alkanoyloxy groups, or 1 to 3  $C_1$ - $C_6$  alkoxy groups;

10

$X^{12}$  is hydrogen,  $C_1$ - $C_6$  alkyl, phenyl, thiazolyl, imidazolyl, furyl, or thienyl, provided that when  $X^{12}$  is not hydrogen, the  $X^{12}$  group is optionally substituted with one to three substituents independently selected from the group consisting of Cl, F,  $CH_3$ ,  $OCH_3$ ,  $OCF_3$ , and  $CF_3$ ;

15

or  $X^{11}$  and  $X^{12}$  are taken together to form  $-(CH_2)_r-L^1-(CH_2)_r-$ , wherein  $L^1$  is  $CX^2X^2$ , O,  $SO_m$ , or  $NX^2$ ;

r for each occurrence is independently 1, 2, or 3;

20  $X^2$  for each occurrence is independently hydrogen, optionally substituted  $C_1$ - $C_6$  alkyl, or optionally substituted  $C_3$ - $C_7$  cycloalkyl, wherein the optionally substituted  $C_1$ - $C_6$  alkyl and optionally substituted  $C_3$ - $C_7$  cycloalkyl in the definition of  $X^2$  are optionally independently substituted with  $-SO_m(C_1$ - $C_6$  alkyl),  $-CO_2X^3$ , 1 to 5 halo groups, or 1-3  $OX^3$  groups;

25  $X^3$  for each occurrence is independently hydrogen or  $C_1$ - $C_6$  alkyl;

$X^6$  for each occurrence is independently hydrogen, optionally substituted  $C_1$ - $C_6$  alkyl, halogenated  $C_2$ - $C_6$  alkyl, optionally substituted  $C_3$ - $C_7$  cycloalkyl, halogenated  $C_3$ - $C_7$  cycloalkyl, wherein the optionally substituted  $C_1$ - $C_6$  alkyl and optionally substituted  $C_3$ - $C_7$  cycloalkyl in the definition of  $X^6$  are optionally independently mono- or di-substituted with  $C_1$ - $C_4$  alkyl, hydroxy,  $C_1$ - $C_4$  alkoxy, carboxyl,  $CONH_2$ ,  $-SO_m(C_1$ - $C_6$  alkyl), carboxylate ( $C_1$ - $C_4$  alkyl) ester, or 1H-tetrazol-5-yl; or

30 when there are two  $X^6$  groups on one atom and both  $X^6$  are independently  $C_1$ - $C_6$  alkyl, the two  $C_1$ - $C_6$  alkyl groups may be optionally joined, and together with the atom to which the two  $X^6$  groups are attached, form a 4- to 9- membered ring optionally having oxygen, sulfur, or  $NX^7$  as a ring member, wherein  $X^7$  is hydrogen or  $C_1$ - $C_6$  alkyl optionally substituted with hydroxy;

m for each occurrence is independently 0, 1, or 2;  
with the provisos that:

$X^6$  and  $X^{12}$  cannot be hydrogen when attached to CO or  $SO_2$  in the form  $COX^6$ ,  $COX^{12}$ ,  $SO_2X^6$  or  $SO_2X^{12}$ ; and

5 when  $R^6$  is a bond then L is  $NX^2$  and each r in the definition  $-(CH_2)_r-L-(CH_2)_r-$  is independently 2 or 3.

16. A pharmaceutical composition according to claim 15 wherein said growth hormone secretagogue is

10 2-amino-N-(2-(3a-(R)-benzyl-2-methyl-3-oxo-2,3,3a,4,6,7-hexahydro-pyrazolo-[4,3-c]pyridin-5-yl)-1-(R)-benzyloxymethyl-2-oxo-ethyl)-isobutyramide;

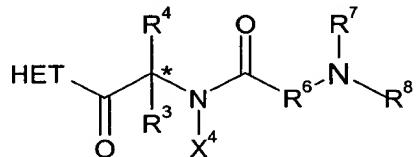
15 2-amino-N-(1-(R)-(2,4-difluoro-benzyloxymethyl)-2-oxo-2-(3-oxo-3a-(R)-pyridin-2-ylmethyl)-2-(2,2,2-trifluoro-ethyl)-2,3,3a,4,6,7-hexahydro-pyrazolo-[4,3-c]pyridin-5-yl)-ethyl)-2-methyl-propionamide;

20 2-amino-N-{1(R)-benzyloxymethyl-2-[1,3-dioxo-8a(S)-pyridin-2-ylmethyl-2-(2,2,2-trifluoro-ethyl)-hexahydro-imidazo[1,5-a]pyrazin-7-yl]-2-oxo-ethyl}-2-methyl-propionamide;

25 N-(1(R)-((1,2-dihydro-1-methanesulfonyl-spiro(3H-indole-3,4'-piperidin)-1'-yl)carbonyl)-2-(phenylmethoxy)ethyl)-2-amino-2-methyl-propanamide; or

a prodrug of any of these compounds or a pharmaceutically acceptable salt of any of said compounds or said prodrugs.

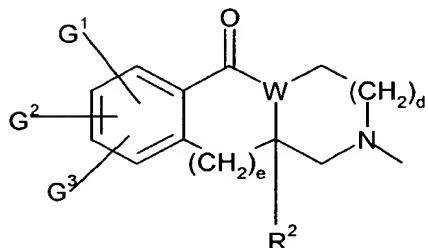
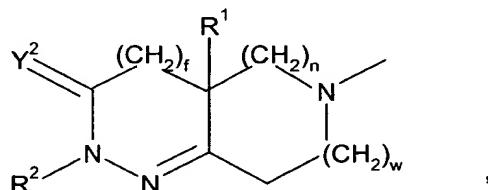
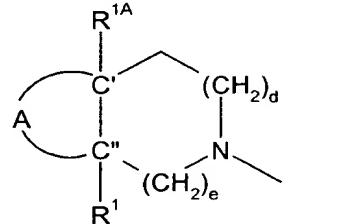
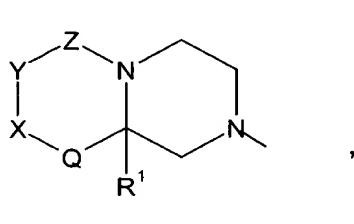
25 17. A pharmaceutical composition according to claim 13 wherein said growth hormone secretagogue is a compound of formula IV:



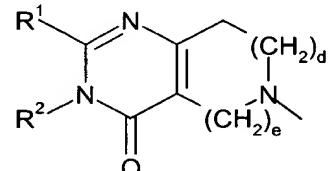
30 or a stereoisomeric mixture thereof, a diastereomerically enriched, diastereomerically pure, enantiomerically enriched, or enantiomerically pure isomer thereof, or a prodrug

of such compound, mixture, or isomer thereof, or a pharmaceutically acceptable salt of the compound, mixture, isomer, or prodrug, wherein:

HET is a heterocyclic moiety selected from the group consisting of



and



5            d is 0, 1, or 2;  
           e is 1 or 2;  
           f is 0 or 1;  
           n and w are 0, 1, or 2, provided that n and w cannot both be 0 at the same time;

10            Y² is oxygen or sulfur;

A is a divalent radical, wherein the left hand side of the radical as shown below is connected to C" and the right hand side of the radical as shown below is connected to C', selected from the group consisting of -NR²-CO-NR²-, -NR²-SO₂-NR²-, -O-CO-NR²-, -NR²-CO₂-, -CO-NR²-CO-, -CO-NR²-C(R⁹R¹⁰)-, -C(R⁹R¹⁰)-NR²-CO-, -C(R⁹R¹⁰)-C(R⁹R¹⁰)-C(R⁹R¹⁰)-, -SO₂-C(R⁹R¹⁰)-C(R⁹R¹⁰)-, -C(R⁹R¹⁰)-O-CO-, -C(R⁹R¹⁰)-O-C(R⁹R¹⁰)-, -NR²-CO-C(R⁹R¹⁰)-, -O-CO-C(R⁹R¹⁰)-, -C(R⁹R¹⁰)-CO-NR²-, -CO-NR²-CO-, -C(R⁹R¹⁰)-CO₂-, -CO-NR²-C(R⁹R¹⁰)-C(R⁹R¹⁰)-, -CO₂-C(R⁹R¹⁰)-, -C(R⁹R¹⁰)-C(R⁹R¹⁰)-C(R⁹R¹⁰)-C(R⁹R¹⁰)-, -SO₂-NR²-C(R⁹R¹⁰)-C(R⁹R¹⁰)-, -C(R⁹R¹⁰)-C(R⁹R¹⁰)-NR²-CO-, -C(R⁹R¹⁰)-C(R⁹R¹⁰)-O-CO-, -NR²-CO-

$C(R^9R^{10})-C(R^9R^{10})-$ ,  $-NR^2-SO_2-C(R^9R^{10})-C(R^9R^{10})-$ ,  $-O-CO-C(R^9R^{10})-C(R^9R^{10})-$ ,  
 $-C(R^9R^{10})-C(R^9R^{10})-CO-NR^2-$ ,  $-C(R^9R^{10})-C(R^9R^{10})-CO-$ ,  $-C(R^9R^{10})-NR^2-CO_2-$ ,  
 $-C(R^9R^{10})-O-CO-NR^2$ ,  $-C(R^9R^{10})-NR^2-CO-NR^2-$ ,  $-NR^2-CO_2-C(R^9R^{10})-$ ,  $-NR^2-CO-NR^2-$   
 $C(R^9R^{10})-$ ,  $-NR^2-SO_2-NR^2-C(R^9R^{10})-$ ,  $-O-CO-NR^2-C(R^9R^{10})-$ ,  $-CO-N=C(R^{11})-NR^2-$ ,  
5  $-CO-NR^2-C(R^{11})=N-$ ,  $-C(R^9R^{10})-NR^{12}-C(R^9R^{10})-$ ,  $-NR^{12}-C(R^9R^{10})-$ ,  $-NR^{12}-C(R^9R^{10})-$   
 $C(R^9R^{10})-$ ,  $-CO_2-C(R^9R^{10})-C(R^9R^{10})-$ ,  $-NR^2-C(R^{11})=N-CO-$ ,  $-C(R^9R^{10})-C(R^9R^{10})-N(R^{12})-$ ,  
 $-C(R^9R^{10})-NR^{12}-$ ,  $-N=C(R^{11})-NR^2-CO-$ ,  $-C(R^9R^{10})-C(R^9R^{10})-NR^2-SO_2-$ ,  $-C(R^9R^{10})-$   
 $C(R^9R^{10})-SO_2-NR^2-$ ,  $-C(R^9R^{10})-C(R^9R^{10})-CO_2-$ ,  $-C(R^9R^{10})-SO_2-C(R^9R^{10})-$ ,  $-C(R^9R^{10})-$   
 $C(R^9R^{10})-SO_2-$ ,  $-O-C(R^9R^{10})-C(R^9R^{10})-$ ,  $-C(R^9R^{10})-C(R^9R^{10})-O-$ ,  $-C(R^9R^{10})-CO-$   
10  $C(R^9R^{10})-$ ,  $-CO-C(R^9R^{10})-C(R^9R^{10})-$ , and  $-C(R^9R^{10})-NR^2-SO_2-NR^2-$ ;

Q is a covalent bond or  $CH_2$ ;

W is CH or N;

X is  $CR^9R^{10}$ ,  $C=CH_2$ , or  $C=O$ ;

Y is  $CR^9R^{10}$ , O, or  $NR^2$ ;

15 Z is  $C=O$ ,  $C=S$ , or  $SO_2$ ;

$G^1$  is hydrogen, halo, hydroxy, nitro, amino, cyano, phenyl, carboxyl,  $-CONH_2$ ,  
 $-C_1-C_4$  alkyl optionally independently substituted with one or more phenyl, one or  
more halogen, or one or more hydroxy groups,  $-C_1-C_4$  alkoxy optionally independently  
substituted with one or more phenyl, one or more halogen, or one or more hydroxy  
20 groups,  $-C_1-C_4$  alkylthio, phenoxy,  $-CO_2-(C_1-C_4$  alkyl), N,N-di-( $C_1-C_4$  alkylamino),  $-C_2-$   
 $C_6$  alkenyl optionally independently substituted with one or more phenyl, one or more  
halogen, or one or more hydroxy groups,  $-C_2-C_6$  alkynyl optionally independently  
substituted with one or more phenyl, one or more halogen, or one or more hydroxy  
25 groups,  $-C_3-C_6$  cycloalkyl optionally independently substituted with one or more  $C_1-C_4$   
alkyl groups, one or more halogen, or one or more hydroxy groups,  $-C_1-C_4$  alkylamino  
carbonyl, or di- $C_1-C_4$  alkylamino carbonyl;

$G^2$  and  $G^3$  are each independently selected from the group consisting of  
hydrogen, halo, hydroxy,  $-C_1-C_4$  alkyl optionally independently substituted with one to  
three halo groups, and  $-C_1-C_4$  alkoxy optionally independently substituted with one to  
30 three halo groups;

$R^1$  is hydrogen,  $-CN$ ,  $-(CH_2)_qNX^6COX^6$ ,  $-(CH_2)_qNX^6CO(CH_2)_lA^1$ ,  
 $-(CH_2)_qNX^6SO_2(CH_2)_lA^1$ ,  $-(CH_2)_qNX^6SO_2X^6$ ,  $-(CH_2)_qNX^6CONX^6(CH_2)_lA^1$ ,  
 $-(CH_2)_qNX^6CONX^6X^6$ ,  $-(CH_2)_qCONX^6X^6$ ,  $-(CH_2)_qCONX^6(CH_2)_lA^1$ ,  $-(CH_2)_qCO_2X^6$ ,  
 $-(CH_2)_qCO_2(CH_2)_lA^1$ ,  $-(CH_2)_qOX^6$ ,  $-(CH_2)_qOCOX^6$ ,  $-(CH_2)_qOCO(CH_2)_lA^1$ ,

-(CH<sub>2</sub>)<sub>q</sub>OCONX<sup>6</sup>(CH<sub>2</sub>)<sub>t</sub>-A<sup>1</sup>, -(CH<sub>2</sub>)<sub>q</sub>OCONX<sup>6</sup>X<sup>6</sup>, -(CH<sub>2</sub>)<sub>q</sub>COX<sup>6</sup>, -(CH<sub>2</sub>)<sub>q</sub>CO(CH<sub>2</sub>)<sub>t</sub>-A<sup>1</sup>, -(CH<sub>2</sub>)<sub>q</sub>NX<sup>6</sup>CO<sub>2</sub>X<sup>6</sup>, -(CH<sub>2</sub>)<sub>q</sub>NX<sup>6</sup>SO<sub>2</sub>NX<sup>6</sup>X<sup>6</sup>, -(CH<sub>2</sub>)<sub>q</sub>SO<sub>m</sub>X<sup>6</sup>, -(CH<sub>2</sub>)<sub>q</sub>SO<sub>m</sub>(CH<sub>2</sub>)<sub>t</sub>-A<sup>1</sup>, -C<sub>1</sub>-C<sub>10</sub> alkyl, -(CH<sub>2</sub>)<sub>t</sub>-A<sup>1</sup>, -(CH<sub>2</sub>)<sub>q</sub>-(C<sub>3</sub>-C<sub>7</sub> cycloalkyl), -(CH<sub>2</sub>)<sub>q</sub>-Y<sup>1</sup>-(C<sub>1</sub>-C<sub>6</sub> alkyl), -(CH<sub>2</sub>)<sub>q</sub>-Y<sup>1</sup>-(CH<sub>2</sub>)<sub>t</sub>-A<sup>1</sup>, or -(CH<sub>2</sub>)<sub>q</sub>-Y<sup>1</sup>-(CH<sub>2</sub>)<sub>t</sub>-(C<sub>3</sub>-C<sub>7</sub> cycloalkyl);

5       wherein the alkyl and cycloalkyl groups in the definition of R<sup>1</sup> are optionally substituted with C<sub>1</sub>-C<sub>4</sub> alkyl, hydroxy, C<sub>1</sub>-C<sub>4</sub> alkoxy, carboxyl, -CONH<sub>2</sub>, -SO<sub>m</sub>-(C<sub>1</sub>-C<sub>6</sub> alkyl), -CO<sub>2</sub>-(C<sub>1</sub>-C<sub>4</sub> alkyl) ester, 1H-tetrazol-5-yl, or 1, 2, or 3 fluoro groups;

10      Y<sup>1</sup> is O, SO<sub>m</sub>, -CONX<sup>6</sup>-, -CH=CH-, -C≡C-, -NX<sup>6</sup>CO-, -CONX<sup>6</sup>-, -CO<sub>2</sub>-, -OCONX<sup>6</sup>- or -OCO-;

      q is 0, 1, 2, 3, or 4;

      t is 0, 1, 2, or 3;

15      said (CH<sub>2</sub>)<sub>q</sub> group and (CH<sub>2</sub>)<sub>t</sub> group in the definition of R<sup>1</sup> are optionally independently substituted with hydroxy, C<sub>1</sub>-C<sub>4</sub> alkoxy, carboxyl, -CONH<sub>2</sub>, -SO<sub>m</sub>-(C<sub>1</sub>-C<sub>6</sub> alkyl), -CO<sub>2</sub>-(C<sub>1</sub>-C<sub>4</sub> alkyl) ester, 1H-tetrazol-5-yl, 1, 2, or 3 fluoro groups, or 1 or 2 C<sub>1</sub>-C<sub>4</sub> alkyl groups;

20      R<sup>1A</sup> is selected from the group consisting of hydrogen, F, Cl, Br, I, C<sub>1</sub>-C<sub>6</sub> alkyl, phenyl-(C<sub>1</sub>-C<sub>3</sub> alkyl), pyridyl-(C<sub>1</sub>-C<sub>3</sub> alkyl), thiazolyl-(C<sub>1</sub>-C<sub>3</sub> alkyl), and thienyl-(C<sub>1</sub>-C<sub>3</sub> alkyl), provided that R<sup>1A</sup> is not F, Cl, Br, or I when a heteroatom is vicinal to C";

25      R<sup>2</sup> is hydrogen, C<sub>1</sub>-C<sub>8</sub> alkyl, -(C<sub>0</sub>-C<sub>3</sub> alkyl)-(C<sub>3</sub>-C<sub>8</sub> cycloalkyl), -(C<sub>1</sub>-C<sub>4</sub> alkyl)-A<sup>1</sup>, or A<sup>1</sup>, wherein the alkyl groups and the cycloalkyl groups in the definition of R<sup>2</sup> are optionally substituted with hydroxy, -CO<sub>2</sub>X<sup>6</sup>, -CONX<sup>6</sup>X<sup>6</sup>, -NX<sup>6</sup>X<sup>6</sup>, -SO<sub>m</sub>(C<sub>1</sub>-C<sub>6</sub> alkyl), -COA<sup>1</sup>, -COX<sup>6</sup>, CF<sub>3</sub>, CN, or 1, 2, or 3 independently selected halo groups;

30      R<sup>3</sup> is selected from the group consisting of A<sup>1</sup>, C<sub>1</sub>-C<sub>10</sub> alkyl, -(C<sub>1</sub>-C<sub>6</sub> alkyl)-A<sup>1</sup>, -(C<sub>1</sub>-C<sub>6</sub> alkyl)-(C<sub>3</sub>-C<sub>7</sub> cycloalkyl), -(C<sub>1</sub>-C<sub>5</sub> alkyl)-X<sup>1</sup>-(C<sub>1</sub>-C<sub>5</sub> alkyl), -(C<sub>1</sub>-C<sub>5</sub> alkyl)-X<sup>1</sup>-(C<sub>0</sub>-C<sub>5</sub> alkyl)-A<sup>1</sup>, and -(C<sub>1</sub>-C<sub>5</sub> alkyl)-X<sup>1</sup>-(C<sub>1</sub>-C<sub>5</sub> alkyl)-(C<sub>3</sub>-C<sub>7</sub> cycloalkyl);

      wherein the alkyl groups in the definition of R<sup>3</sup> are optionally substituted with -SO<sub>m</sub>(C<sub>1</sub>-C<sub>6</sub> alkyl), -CO<sub>2</sub>X<sup>3</sup>, 1, 2, 3, 4, or 5 independently selected halo groups, or 1, 2, or 3 independently selected -OX<sup>3</sup> groups;

35      X<sup>1</sup> is O, SO<sub>m</sub>, -NX<sup>2</sup>CO-, -CONX<sup>2</sup>-, -OCO-, -CO<sub>2</sub>-, -CX<sup>2</sup>=CX<sup>2</sup>-, -NX<sup>2</sup>CO<sub>2</sub>-, -OCONX<sup>2</sup>-, or -C≡C-;

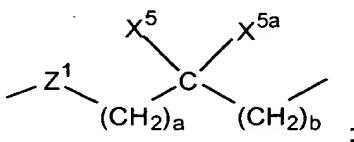
40      R<sup>4</sup> is hydrogen, C<sub>1</sub>-C<sub>6</sub> alkyl, or C<sub>3</sub>-C<sub>7</sub> cycloalkyl, or R<sup>4</sup> taken together with R<sup>3</sup> and the carbon atom to which they are attached form C<sub>5</sub>-C<sub>7</sub> cycloalkyl, C<sub>5</sub>-C<sub>7</sub> cycloalkenyl, a partially saturated or fully saturated 4- to 8-membered ring having 1 to

4 heteroatoms independently selected from the group consisting of oxygen, sulfur, and nitrogen, or a bicyclic ring system consisting of a partially saturated or fully saturated 5- or 6-membered ring, fused to a partially saturated, fully unsaturated, or fully saturated 5- or 6-membered ring, optionally having 1 to 4 heteroatoms  
5 independently selected from the group consisting of nitrogen, sulfur, and oxygen;

X<sup>4</sup> is hydrogen or C<sub>1</sub>-C<sub>6</sub> alkyl, or X<sup>4</sup> is taken together with R<sup>4</sup> and the nitrogen atom to which X<sup>4</sup> is attached and the carbon atom to which R<sup>4</sup> is attached and form a five to seven membered ring;

R<sup>6</sup> is a bond or is

10



wherein a and b are each independently 0, 1, 2, or 3;

X<sup>5</sup> and X<sup>5a</sup> are each independently selected from the group consisting of hydrogen, CF<sub>3</sub>, A<sup>1</sup>, and C<sub>1</sub>-C<sub>6</sub> alkyl optionally substituted with A<sup>1</sup>, OX<sup>2</sup>, -  
15 SO<sub>m</sub>-(C<sub>1</sub>-C<sub>6</sub> alkyl), -CO<sub>2</sub>X<sup>2</sup>, C<sub>3</sub>-C<sub>7</sub> cycloalkyl, -NX<sup>2</sup>X<sup>2</sup>, or -CONX<sup>2</sup>X<sup>2</sup>;

20 or the carbon bearing X<sup>5</sup> or X<sup>5a</sup> forms one or two alkylene bridges with the nitrogen atom bearing R<sup>7</sup> and R<sup>8</sup> wherein each alkylene bridge contains 1 to 5 carbon atoms, provided that when one alkylene bridge is formed then only one of X<sup>5</sup> or X<sup>5a</sup> is on the carbon atom and only one of R<sup>7</sup> or R<sup>8</sup> is on the nitrogen atom, and further provided that when two alkylene bridges are formed then X<sup>5</sup> and X<sup>5a</sup> cannot be on the carbon atom and R<sup>7</sup> and R<sup>8</sup> cannot be on the nitrogen atom;

25 or X<sup>5</sup> taken together with X<sup>5a</sup> and the carbon atom to which they are attached form a partially saturated or fully saturated 3- to 7-membered ring, or a partially saturated or fully saturated 4- to 8-membered ring having 1 to 4 heteroatoms independently selected from the group consisting of oxygen, sulfur, and nitrogen;

30 or X<sup>5</sup> taken together with X<sup>5a</sup> and the carbon atom to which they are attached form a bicyclic ring system consisting of a partially saturated or fully saturated 5- or 6-membered ring, optionally having 1 or 2 heteroatoms independently selected from the group consisting of nitrogen, sulfur, and

oxygen, fused to a partially saturated, fully saturated, or fully unsaturated 5- or 6-membered ring, optionally having 1 to 4 heteroatoms independently selected from the group consisting of nitrogen, sulfur, and oxygen;

5             $Z^1$  is a bond, O, or  $N-X^2$ , provided that when a and b are both 0 then  $Z^1$  is not  $N-X^2$  or O;

$R^7$  and  $R^8$  are each independently hydrogen or  $C_1-C_6$  alkyl optionally independently substituted with  $A^1$ ,  $-CO_2-(C_1-C_6$  alkyl),  $-SO_m(C_1-C_6$  alkyl), 1 to 5 halo groups, 1 to 3 hydroxy groups, 1 to 3  $-O-CO(C_1-C_{10}$  alkyl) groups, or 1 to 3  $C_1-C_6$  alkoxy groups; or

10            $R^7$  and  $R^8$  can be taken together to form  $-(CH_2)_r-L-(CH_2)_r$ , wherein L is  $CX^2X^2$ ,  $SO_m$ , or  $NX^2$ ;

$R^9$  and  $R^{10}$  are each independently selected from the group consisting of hydrogen, fluoro, hydroxy, and  $C_1-C_5$  alkyl optionally independently substituted with 1-5 halo groups;

15            $R^{11}$  is selected from the group consisting of  $C_1-C_5$  alkyl and phenyl optionally substituted with 1-3 substituents each independently selected from the group consisting of  $C_1-C_5$  alkyl, halo, and  $C_1-C_5$  alkoxy;

20            $R^{12}$  is selected from the group consisting of  $C_1-C_5$  alkylsulfonyl,  $C_1-C_5$  alkanoyl, and  $C_1-C_5$  alkyl wherein the alkyl portion is optionally independently substituted by 1-5 halo groups;

$A^1$  for each occurrence is independently selected from the group consisting of  $C_5-C_7$  cycloalkenyl, phenyl, a partially saturated, fully saturated, or fully unsaturated 4- to 8-membered ring optionally having 1 to 4 heteroatoms independently selected from the group consisting of oxygen, sulfur, and nitrogen, and a bicyclic ring system 25 consisting of a partially saturated, fully unsaturated, or fully saturated 5- or 6-membered ring, optionally having 1 to 4 heteroatoms independently selected from the group consisting of nitrogen, sulfur, and oxygen, fused to a partially saturated, fully saturated, or fully unsaturated 5- or 6-membered ring, optionally having 1 to 4 heteroatoms independently selected from the group consisting of nitrogen, sulfur, and oxygen; and

30           oxygen;

$A^1$  for each occurrence is independently optionally substituted, on one or optionally both rings if  $A^1$  is a bicyclic ring system, with up to three substituents, each substituent independently selected from the group consisting of F, Cl, Br, I,  $OCF_3$ ,  $OCF_2H$ ,  $CF_3$ ,  $CH_3$ ,  $OCH_3$ ,  $-OX^6$ ,  $-CONX^6X^6$ , -

CO<sub>2</sub>X<sup>6</sup>, oxo, C<sub>1</sub>-C<sub>6</sub> alkyl, nitro, cyano, benzyl, -SO<sub>m</sub>(C<sub>1</sub>-C<sub>6</sub> alkyl), 1H-tetrazol-5-yl, phenyl, phenoxy, phenylalkyloxy, halophenyl, methylenedioxy, -NX<sup>6</sup>X<sup>6</sup>, -NX<sup>6</sup>COX<sup>6</sup>, -SO<sub>2</sub>NX<sup>6</sup>X<sup>6</sup>, -NX<sup>6</sup>SO<sub>2</sub>-phenyl, NX<sup>6</sup>SO<sub>2</sub>X<sup>6</sup>, -CONX<sup>11</sup>X<sup>12</sup>, -SO<sub>2</sub>NX<sup>11</sup>X<sup>12</sup>, -NX<sup>6</sup>SO<sub>2</sub>X<sup>12</sup>, -NX<sup>6</sup>CONX<sup>11</sup>X<sup>12</sup>, -NX<sup>6</sup>SO<sub>2</sub>NX<sup>11</sup>X<sup>12</sup>, -NX<sup>6</sup>COX<sup>12</sup>, 5 imidazolyl, thiazolyl, and tetrazolyl, provided that if A<sup>1</sup> is optionally substituted with methylenedioxy then it can only be substituted with one methylenedioxy;

10 wherein X<sup>11</sup> is hydrogen or C<sub>1</sub>-C<sub>6</sub> alkyl optionally independently substituted with phenyl, phenoxy, C<sub>1</sub>-C<sub>6</sub> alkoxy carbonyl, -SO<sub>m</sub>(C<sub>1</sub>-C<sub>6</sub> alkyl), 1 to 5 halo groups, 1 to 3 hydroxy groups, 1 to 3 C<sub>1</sub>-C<sub>10</sub> alkanoyloxy groups, or 1 to 3 C<sub>1</sub>-C<sub>6</sub> alkoxy groups;

15 X<sup>12</sup> is hydrogen, C<sub>1</sub>-C<sub>6</sub> alkyl, phenyl, thiazolyl, imidazolyl, furyl, or thienyl, provided that when X<sup>12</sup> is not hydrogen, the X<sup>12</sup> group is optionally substituted with one to three substituents independently selected from the group consisting of Cl, F, CH<sub>3</sub>, OCH<sub>3</sub>, OCF<sub>3</sub>, and CF<sub>3</sub>;

or X<sup>11</sup> and X<sup>12</sup> are taken together to form -(CH<sub>2</sub>)<sub>r</sub>-L<sup>1</sup>-(CH<sub>2</sub>)<sub>r</sub>-, wherein L<sup>1</sup> is CX<sup>2</sup>X<sup>2</sup>, O, SO<sub>m</sub>, or NX<sup>2</sup>;

r for each occurrence is independently 1, 2, or 3;

20 X<sup>2</sup> for each occurrence is independently hydrogen, optionally substituted C<sub>1</sub>-C<sub>6</sub> alkyl, or optionally substituted C<sub>3</sub>-C<sub>7</sub> cycloalkyl, wherein the optionally substituted C<sub>1</sub>-C<sub>6</sub> alkyl and optionally substituted C<sub>3</sub>-C<sub>7</sub> cycloalkyl in the definition of X<sup>2</sup> are optionally independently substituted with -SO<sub>m</sub>(C<sub>1</sub>-C<sub>6</sub> alkyl), -CO<sub>2</sub>X<sup>3</sup>, 1 to 5 halo groups, or 1-3 OX<sup>3</sup> groups;

25 X<sup>3</sup> for each occurrence is independently hydrogen or C<sub>1</sub>-C<sub>6</sub> alkyl;

X<sup>6</sup> for each occurrence is independently hydrogen, optionally substituted C<sub>1</sub>-C<sub>6</sub> alkyl, halogenated C<sub>2</sub>-C<sub>6</sub> alkyl, optionally substituted C<sub>3</sub>-C<sub>7</sub> cycloalkyl, halogenated C<sub>3</sub>-C<sub>7</sub> cycloalkyl, wherein the optionally substituted C<sub>1</sub>-C<sub>6</sub> alkyl and optionally substituted C<sub>3</sub>-C<sub>7</sub> cycloalkyl in the definition of X<sup>6</sup> are optionally independently mono- or di-substituted with C<sub>1</sub>-C<sub>4</sub> alkyl, hydroxy, C<sub>1</sub>-C<sub>4</sub> alkoxy, carboxyl, CONH<sub>2</sub>, -SO<sub>m</sub>(C<sub>1</sub>-C<sub>6</sub> alkyl), carboxylate (C<sub>1</sub>-C<sub>4</sub> alkyl) ester, or 1H-tetrazol-5-yl; or

30 when there are two X<sup>6</sup> groups on one atom and both X<sup>6</sup> are independently C<sub>1</sub>-C<sub>6</sub> alkyl, the two C<sub>1</sub>-C<sub>6</sub> alkyl groups may be optionally joined, and together with the atom to which the two X<sup>6</sup> groups are attached, form a 4- to 9- membered ring

optionally having oxygen, sulfur, or NX<sup>7</sup> as a ring member, wherein X<sup>7</sup> is hydrogen or C<sub>1</sub>-C<sub>6</sub> alkyl optionally substituted with hydroxy;

m for each occurrence is independently 0, 1, or 2;

with the provisos that:

5        X<sup>6</sup> and X<sup>12</sup> cannot be hydrogen when attached to CO or SO<sub>2</sub> in the form COX<sup>6</sup>, COX<sup>12</sup>, SO<sub>2</sub>X<sup>6</sup> or SO<sub>2</sub>X<sup>12</sup>; and

when R<sup>6</sup> is a bond then L is NX<sup>2</sup> and each r in the definition -(CH<sub>2</sub>)<sub>r</sub>-L-(CH<sub>2</sub>)<sub>r</sub> is independently 2 or 3.

10        18. A pharmaceutical composition according to claim 17 wherein said growth hormone secretagogue is

2-amino-N-(2-(3a-(R)-benzyl-2-methyl-3-oxo-2,3,3a,4,6,7-hexahydro-pyrazolo-[4,3-c]pyridin-5-yl)-1-(R)-benzyloxymethyl-2-oxo-ethyl)-isobutyramide;

15        2-amino-N-(1-(R)-(2,4-difluoro-benzyloxymethyl)-2-oxo-2-(3-oxo-3a-(R)-pyridin-2-ylmethyl)-2-(2,2,2-trifluoro-ethyl)-2,3,3a,4,6,7-hexahydro-pyrazolo-[4,3-c]pyridin-5-yl)-ethyl)-2-methyl-propionamide;

20        2-amino-N-{1(R)-benzyloxymethyl-2-[1,3-dioxo-8a(S)-pyridin-2-ylmethyl-2-(2,2,2-trifluoro-ethyl)-hexahydro-imidazo[1,5-a]pyrazin-7-yl]-2-oxo-ethyl}-2-methyl-propionamide;

N-(1(R)-((1,2-dihydro-1-methanesulfonyl-spiro(3H-indole-3,4'-piperidin)-1'-yl)carbonyl)-2-(phenylmethoxy)ethyl)-2-amino-2-methyl-propanamide; or

25        a prodrug of any of these compounds, or a pharmaceutically acceptable salt of any of these compounds or prodrugs.

19. A pharmaceutical composition according to claim 18 wherein said corticotropin releasing factor antagonist is 4-(1-ethyl-propoxy)-3,6-dimethyl-2-(2,4,6-trimethylphenoxy)-pyridine and said growth hormone secretagogue is 2-amino-N-[2-(3a(R)-benzyl-2-methyl-3-oxo-2,3,3a,4,6,7-hexahydro-pyrazolo-[4,3-c]pyridin-5-yl)-1(R)-benzyloxymethyl-2-oxo-ethyl]-isobutyramide.

20. A pharmaceutical composition according to claim 18 wherein said corticotropin releasing factor antagonist is 4-(1-ethyl-propoxy)-3,6-dimethyl-2-(2,4,6-

trimethylphenoxy)-pyridine and said growth hormone secretagogue is 2-amino-N-(1(R)-(2,4-difluoro-benzyloxymethyl)-2-oxo-2-(3-oxo-3a(R)-(pyridin-2-ylmethyl)-2-(2,2,2-trifluoro-ethyl)-2,3,3a,4,6,7-hexahydro-pyrazolo-[4,3-c]pyridin-5-yl)-ethyl)-2-methyl-propionamide.

5

21. A pharmaceutical composition according to claim 18 wherein said corticotropin releasing factor antagonist is (3,6-dimethyl-2-(2,4,6-trimethyl-phenoxy)-pyridin-4-yl)-(1-ethyl-propyl)-amine and said growth hormone secretagogue is 2-amino-N-[2-(3a(R)-benzyl-2-methyl-3-oxo-2,3,3a,4,6,7-hexahydro-pyrazolo-[4,3-c]pyridin-5-yl)-1(R)-benzyloxymethyl-2-oxo-ethyl]-isobutyramide.

10

22. A pharmaceutical composition according to claim 18 wherein said corticotropin releasing factor antagonist is (3,6-dimethyl-2-(2,4,6-trimethyl-phenoxy)-pyridin-4-yl)-(1-ethyl-propyl)-amine and said growth hormone secretagogue is 2-amino-N-(1(R)-(2,4-difluoro-benzyloxymethyl)-2-oxo-2-(3-oxo-3a(R)-(pyridin-2-ylmethyl)-2-(2,2,2-trifluoro-ethyl)-2,3,3a,4,6,7-hexahydro-pyrazolo-[4,3-c]pyridin-5-yl)-ethyl)-2-methyl-propionamide.

15

23. A method for treating or preventing osteoporosis or frailty associated with aging or obesity, said method comprising administering to a human or other animal an amount of a pharmaceutical composition according to claim 1, which is effective in treating or preventing osteoporosis or frailty associated with aging or obesity.

20

24. A method for treating or preventing a cardiovascular or heart related disease, said method comprising administering to a human or other animal an amount of a pharmaceutical composition according to claim 1, which is effective in treating or preventing the cardiovascular or heart related disease.

25

25. A method according to claim 24 wherein the cardiovascular or heart related disease is hypertension, tachycardia, or congestive heart failure.

26. A method for accelerating bone fracture repair, attenuating protein catabolic response after a major operation, reducing cachexia and protein loss due to

chronic illness, accelerating wound healing, or accelerating the recovery of burn patients or of patients having undergone major surgery, said method comprising administering to a human or other animal an amount of a pharmaceutical composition according to claim 1, which is effective in accelerating bone fracture repair,  
5 attenuating protein catabolic response after a major operation, reducing cachexia and protein loss due to chronic illness, accelerating wound healing, or accelerating the recovery of burn patients or of patients having undergone major surgery.

27. A method for treating or preventing osteoporosis, frailty associated  
10 with aging or obesity, cardiovascular or heart related disease, for accelerating bone fracture repair, attenuating protein catabolic response after a major operation, reducing cachexia and protein loss due to chronic illness, accelerating wound healing, or accelerating the recovery of burn patients or of patients having undergone major surgery, said method comprising administering to a human or other animal an  
15 amount of a corticotropin releasing factor antagonist and an amount of a growth hormone secretagogue or growth hormone.

28. The method of claim 27 wherein said corticotropin releasing factor antagonist and said growth hormone secretagogue or growth hormone are  
20 administered simultaneously or in a specifically timed manner.

29. A kit comprising:  
a. an amount of a corticotropin releasing factor antagonist, in a  
first unit dosage form;  
25 b. an amount of a growth hormone secretagogue or growth  
hormone, in a second unit dosage form; and  
c. a container.

30. A kit comprising:  
a. an amount of a corticotropin releasing factor antagonist as  
defined in claim 13, in a first unit dosage form;  
b. an amount of a growth hormone secretagogue or growth  
hormone, in a second unit dosage form; and  
c. a container.

31. A kit comprising:

- a. an amount of a corticotropin releasing factor antagonist as defined in claim 14, in a first unit dosage form;
- 5 b. an amount of a growth hormone secretagogue or growth hormone, in a second unit dosage form; and
- c. a container.

32. A kit comprising:

- 10 a. an amount of a corticotropin releasing factor antagonist, in a first unit dosage form;
- b. an amount of a growth hormone secretagogue as defined in claim 15, in a second unit dosage form; and
- c. a container.

15 33. A kit according to claim 29 wherein said corticotropin releasing factor antagonist is 4-(1-ethyl-propoxy)-3,6-dimethyl-2-(2,4,6-trimethylphenoxy)-pyridine or [3,6-dimethyl-2-(2,4,6-trimethyl-phenoxy)-pyridin-4-yl]-(1-ethyl-propyl)-amine, and said growth hormone secretagogue is 2-amino-N-[2-(3a(R)-benzyl-2-methyl-3-oxo-20 2,3,3a,4,6,7-hexahydro-pyrazolo-[4,3-c]pyridin-5-yl)-1(R)-benzyloxymethyl-2-oxo-ethyl]-isobutyramide or 2-amino-N-(1-(R)-(2,4-difluoro-benzyloxymethyl)-2-oxo-2-(3-oxo-3a-(R)-pyridin-2-ylmethyl)-2-(2,2,2-trifluoro-ethyl)-2,3,3a,4,6,7-hexahydro-pyrazolo-[4,3-c]pyridin-5-yl)-ethyl)-2-methyl-propionamide.

25 34. A kit, comprising

- a. a pharmaceutical composition, comprising an amount of a growth hormone or growth hormone secretagogue;
- b. a package containing the above composition; and
- c. a package insert that may be integral with said package;

30 wherein it is stated on the package insert that the pharmaceutical composition is to be administered simultaneously or in a specifically timed manner with a pharmaceutical composition containing at least one corticotropin releasing factor antagonist.

35. A kit, comprising

- a. a pharmaceutical composition, comprising an amount of a corticotropin releasing factor antagonist;
- b. a package containing the above composition; and
- c. a package insert that may be integral with said package;

5 wherein it is stated on the package insert that the pharmaceutical composition is to be administered simultaneously or in a specifically timed manner with a pharmaceutical composition containing at least one growth hormone or growth hormone secretagogue.